



City of Hope®

CITYNEWS

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Sea Change

After a multiple myeloma diagnosis, an Orange County patient finds a new outlook

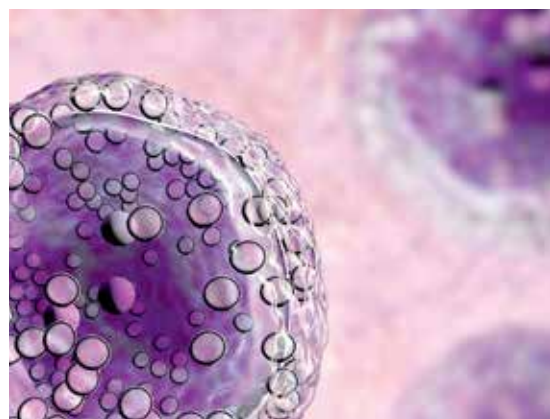


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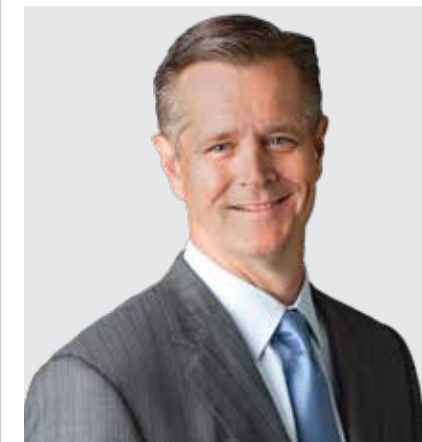


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LEADERSHIP MESSAGE

KNOWLEDGE + IMAGINATION WILL CHANGE THE WORLD

At City of Hope, we believe that knowledge is quickly becoming unlimited and, coupled with imagination, will change the world.

Medical knowledge has expanded exponentially in the 21st century. While researchers estimate that it took 50 years for medical knowledge to double in 1950, that doubling time accelerated to seven years in 1980, and took only three and a half years in 2010. Clinical researchers project that medical knowledge will double in 73 days by 2020.

This vast amount of medical information and intelligence is propelling medicine forward at a remarkable pace, resulting in research breakthroughs, disruptive technologies and therapies targeted at life's most serious illnesses.

City of Hope is at the center of these innovations, translating revolutionary discoveries into life-changing treatments for patients around the world.

In this issue of City News, you will see how we are driving the science that helps cancer survivors like Donna McNutt hold onto hope after a life-threatening diagnosis. You will learn how we are pioneering novel therapeutics and prognostics to prevent, detect and treat lymphoma, most recently earning an extraordinary \$12.5 million grant from the National Cancer Institute. You will read about our leadership in “theranostics” – therapy combined with diagnostics – in which we identify and treat cancer at the same time.

Since our beginnings more than 100 years ago, we have been dedicated to combining the best science with selflessness and compassion. We thank you for your commitment to helping us deliver the next generation of cancer and diabetes cures and care.

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



City of Hope is transforming the future of health. Every day we turn science into practical benefit. We turn hope into reality. We accomplish this through exquisite care, innovative research and vital education focused on eliminating cancer and diabetes. © 2012 City of Hope

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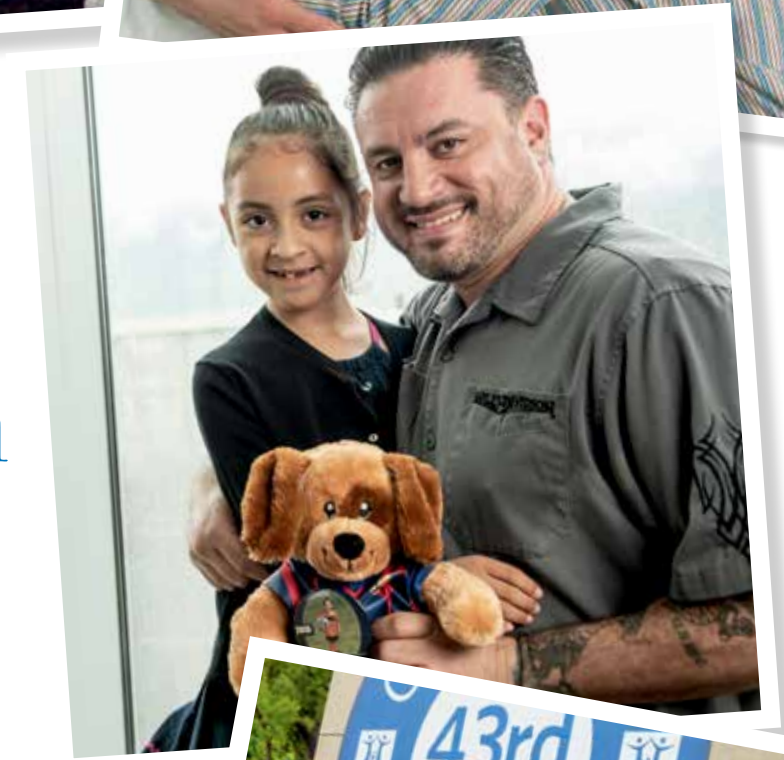
Your Thoughts, Your Wishes, Your Community
Where those touched by cancer can be connected,
survive and thrive together.

cityBUZZ



43rd Bone Marrow Transplant Reunion

At City of Hope's 43rd annual Bone Marrow Transplant Reunion, held on May 10, an 8-year-old acute lymphoblastic leukemia patient, Zuleika Flores (right), had the opportunity to thank the donor who gave her a second chance at life. Also at the event, acute myeloid leukemia patient Leif Voeltz hugged the man who gave him a lifesaving donation, all the way from Germany (top right).



Each year, City of Hope invites bone marrow transplant recipients and their families to attend the annual "Celebration of Life" event on the Duarte, California, campus. The reunion has grown to more than 6,500 attendees from all over the United States and overseas.



cityBUZZ

NURSING WEEK

Each year, National Nurses Week is observed May 6 through 12, ending on the birthday of Florence Nightingale, the founder of modern nursing. This year, the theme for Nurses Week was "Nurses: Inspire, Innovate, Influence." To honor our nurses, who are the heart of City of Hope, we provided food, gifts, pampering and awards throughout the week to let each and every nurse know how much they are appreciated.



Michael Amini Transfusion Medicine Center Celebrates 10 Years

On June 19, friends of City of Hope celebrated the 10th anniversary of the Michael Amini Transfusion Medicine Center.

Ten years ago, donors of blood and platelets lined up outside temporary modular facilities at City of Hope to donate. A visionary gift from Michael Amini led the way for the construction of a new, centralized state-of-the-art blood donation and cell-processing facility that opened in 2009 and bears his name.

Nearly everyone who comes to City of Hope for treatment will spend time at the Amini Center. It is home to blood collection and storage, bone marrow transplantation and cell processing. It is a hub for the activities associated with most cancer treatment and the cellular therapies underlying dozens of clinical trials at City of Hope.

The impact of one man's gift continues to be felt as lives are transformed every day by the work being done at the Amini Center.



From left to right: Sahar Amini, Iman Amini, Nafice Amini, Lily Amini, Michael Amini, Bauhaur Amini, Martin Ploy, Jane Seymour, Robert Stone, Vijay Trisal, M.D.

newHOPE

NEW FACES • ADVANCING SCIENCE • BEGINNINGS

Lorna Rodriguez-Rodriguez, M.D., Ph.D.

For more than 30 years, Lorna Rodriguez-Rodriguez, M.D., Ph.D., has been a standout in gynecological oncology. Specializing in ovarian cancer, she has served as clinician, instructor and researcher at several of America's leading medical institutions.

Her interest in medicine began when, as a child, she watched as doctors cared for her chronically ill brother. "I wanted to be one of them," she recalled, "so I could help people when they felt hopeless ... I wanted to be both a scientist that would make discoveries and find new cures, and a physician who could alleviate the pain of illness."

Consistently rated one of "America's Top Doctors", Rodriguez-Rodriguez spent two decades leading the Gynecologic Oncology Department at Rutgers Cancer Institute of New Jersey.

A noted researcher, Rodriguez-Rodriguez is eagerly continuing her ovarian cancer investigations at City of Hope, which she calls "the perfect environment" that's home to "many amazing scientists and clinicians [with] similar goals about making discoveries to cure cancer."

Rodriguez-Rodriguez will provide oversight to the Markel-Friedman Accelerator Fund for Ovarian and Peritoneal Cancer.



investiture Highlights

Jianjun Chen, Ph.D.

As a child living in a small village in the Hunan Province of China, celebrated scientist Jianjun Chen, Ph.D., professor and vice chair of the Department of Systems Biology, knew even then that his career interests would take him to the other side of the world.

His global journey led him to City of Hope two years ago, and recently that journey culminated in his investiture as the Simms/Mann Family Foundation Chair in Systems Biology. Chen was recognized with the endowment for his leading-edge cancer research that is founded in personalized, gene-based medicine.

"Dr. Jianjun Chen is digging into the very DNA of cancer," said City of Hope President and CEO Robert Stone. "The complex, coded instructions that determine when and how cancer starts, the triggers that set the whole process in motion and the techniques that stop it in its tracks. Dr. Victoria Mann Simms and Ronald Simms are visionary philanthropists who share our sense of urgency and mission to serve the whole patient — body and soul. With their support, we are able to hasten innovative research that puts cures for patients into doctors' hands more quickly."



From left to right: Jianjun Chen, Ph.D., Dr. Victoria Mann Simms, Ronald Simms, Xiaolan Deng, Ph.D. (Chen's wife)

Dreaming, Fighting, Hoping

After Myeloma Diagnosis

BY STEPHANIE SMITH

“We got your bone marrow back and there were so many cancer cells, they quit counting.”

Donna McNutt remembers very little about the Easter day four years ago when she first found out she had cancer — except some stinging words from the oncologist.

“I think back now and it’s almost like I’m watching a movie,” said McNutt, who was 54 when she was diagnosed.

“I do remember this — I said, ‘Could you tell me how long I have to live?’ And the oncologist said, ‘Well, I think I could buy you five years.’”

*Click here to watch
Donna’s story*



*McNutt and her husband, Jack,
near their home in Laguna Beach*

The doctor continued. McNutt’s normal blood cell production had been choked off and overwhelmed by cancer — at least 85% of her marrow was myeloma. She also had calcium dumping into her bloodstream, failing kidneys and four broken ribs.

Pain had begun creeping into her midsection several weeks earlier. It sank deeper and deeper until her entire ribcage throbbed. At one point McNutt, on her mother’s advice, wrapped herself in medicated arthritis patches to soothe the pain. “It was almost comical how many I had on me,” she said.

“For six weeks I walked around with dwindling ribs,” said McNutt, now 58, who lives with her family in Laguna Beach, California. “I probably broke two at a time and even now I think, ‘How did I walk around like that?’ Broken ribs are so painful.”

That sobering inventory — hypercalcemia (high blood calcium), renal problems, anemia and bone problems, also known by the acronym C.R.A.B. — reflects the typical symptoms of multiple myeloma. It is a relatively rare blood cancer, expected to affect about 32,000 people in 2019, according to the American Cancer Society.

McNutt was diagnosed with Stage 4 disease.

She languished in the hospital for several days following her diagnosis. “I looked like a bloated, broken 90-year-old woman,” she said. “I couldn’t even move — I could not move. I was in so much pain.”

McNutt’s family — her husband, Jack, and her three children, Corbin, Hunter and Tatum — huddled close by. Her husband remembers how he felt when the oncologist put his wife’s survival at five years.

“I remember thinking, ‘I can’t believe my wife has an expiration date all of a sudden,’” he said. “I mean, we never know when we’re going to die, but to have an expiration date to say you are going to die.

“It was just sad, sad ... thinking about that.”

McNutt’s daughter, Tatum, who was then 15, felt sadness well up after her first hospital visit. Up to that point, no one had sat her down to fully explain things. All she knew was the worst-case scenario being painted on the internet. According to websites she read, the chances of her mom dying within six months were “10 out of 10.”

After leaving the hospital, Tatum remembers feeling overwhelmed and anxious, like her world was crumbling. “My first thought was I’m never having kids,” said Tatum. “I told my boyfriend, ‘I’m too afraid to have kids without my mom.’”

It took several days — of crying, of rationalizing, of grounding, of purging negative emotions — before the family could shrug off feeling terrified. Armed with a healthier level of fear, the McNutt family decided they would fight for more than



Donna McNutt

“I will keep fighting. I will not let cancer take the drive and the goals I have. I can still dream.”

the six-month prognosis suggested on the internet — more than the five years from the Orange County oncologist.

Around the same time, a piece of advice surfaced from the barrage coming from friends and family. A friend who was a cancer survivor spoke highly about a hematologist-oncologist and myeloma specialist at City of Hope who had treated her: Amrita Krishnan, M.D.

Jack McNutt made a mental note.

A day later, McNutt’s oncologist in Orange County mentioned she was collaborating with Krishnan. It felt like an omen.

“It felt like we were in the right hands,” said Jack McNutt. “After that, I made my decision for Donna and I. We’re taking this path — done.”

McNutt arrived at City of Hope several weeks later. Soon afterward, she got a stem cell transplant, effectively killing off any visible trace of myeloma in her body.

Sitting in the family’s cozy cottage in Laguna Beach on a rare stormy day in January 2017 — two years removed from her transplant — McNutt was philosophical about what she and other cancer patients refer to as, “The Cancer Journey.”

The storm whipping the outside of her home was, in some ways, a metaphor for the cancer that raged in her body and the impact it continued to have on the family. They will weather these storms — at least until a cure is found for myeloma.

Then, McNutt’s concern was about a bone marrow aspiration she would have in a few days; a painful extraction of her bone marrow to test for cancer. Tomorrow it will be something else.

McNutt says that cancer will always loom over her — her disease does not have a cure, so she will likely be on maintenance therapy for the rest of her life. But one thing cancer has done that she did not expect: It has cast a sheen over every interaction she has, especially with her family.

“I believe my relationships are the best they’ve ever been because I don’t wait till tomorrow to say something that I need to say today.”

Awaiting the results of tests like these, going through emotional ups-and-downs, reminds McNutt how tenuous her situation is. But it also somehow buoys her.

“The biggest thing I’ve learned, more than my body failing me, is that my mind has played such an important role on this journey,” said McNutt. “Keeping one step ahead in my mind every time I have a setback in my body. I will keep fighting. I will not let cancer take the drive and the goals I have. I can still dream.

“I can still dream.”

Dreaming, fighting — holding on to hope — and the fast pace of myeloma research at City of Hope and other institutions, is what the McNutt family hopes will keep Donna McNutt here for many years to come.

City of Hope Reveals Vision for World-class Cancer Care in Orange County

Very soon, patients like Donna McNutt of Laguna Beach, California, will be able to access City of Hope physicians close to home. City of Hope has accelerated its plans for a \$1 billion comprehensive cancer campus in Orange County, bringing highly specialized cancer care, clinical trials, precision medicine and early detection to the nation’s sixth most populous county.

The state-of-the art campus in Irvine, California, is expected to open in 2021 — sooner than initially planned. The initiative is part of City of Hope’s commitment to speeding pioneering treatments and scientific breakthroughs to the people who need them today.

Last year, City of Hope and FivePoint Holdings, LLC, the largest developer of mixed-use, master-planned communities in coastal California, announced their partnership to build a \$200 million, 73,000-square-foot cancer center in Irvine. The center, in FivePoint’s Great Park Neighborhoods, was slated to open in 2025.

As planning progressed, FivePoint and City of Hope expanded their vision for the Great Park as a model community of the future with easily accessible world-class health and wellness as a core offering. In line with this vision, City of Hope significantly increased its investment with a focus on highly specialized cancer care, research and lifesaving treatments.

Now a space as big as the vision, the cancer campus on approximately 11 acres will include an existing building of approximately 190,000 square feet that will be a center of innovative cancer research and treatment. This increased investment will enable the campus to open its doors by 2021.

City of Hope officials cite several reasons for an expanded presence in the region. Nearly 20% of residents leave the area for advanced care, with many heading to City of Hope’s main campus in Duarte — up to a two-hour commute away. And despite its reputation for healthy living, Orange County is not immune from the 1-in-3 national statistic for cancer incidence. In fact, the cancer incidence rate in the county is projected to increase by 18% over the next decade. Cancer risk increases with age, and the county’s population is aging faster than the U.S. average.

“We’ve spent the last year listening intently to the people in Orange

County, evaluating the services needed now and in the future and identifying the gaps,” said Annette M. Walker, president of City of Hope Orange County. “It became evident that we needed to bring our highly specialized treatments as soon as possible. We’re delivering on our promise and opening our doors faster to alleviate the unnecessary hardships on patients and their families.”

The new City of Hope cancer campus will include:

- Orange County’s only specialty hospital dedicated solely to treating and curing cancer
- An outpatient cancer center offering diagnostic imaging and screenings, precision medicine and early detection, medical oncology, chemotherapy, radiation therapy, surgical oncology and ambulatory surgery
- A clinical research center offering phase 1-3 clinical trials
- Personalized supportive care services that include palliative care physicians, psychiatrists, social workers and others who partner with patients and their families to address the many physical and emotional issues that can arise during and after treatment
- Access to a wide range of solid tumor and blood cancer specialists dedicated to finding the best treatments for each patient

“This is a time of great promise and innovation in cancer research and care, and we are bringing that excitement and expertise to Orange County,” said Robert Stone, president and CEO of City of Hope. “City of Hope is dramatically expanding to provide a cancer network of unparalleled scale for this community.”

As City of Hope makes significant investments in Orange County health care, enterprise leaders will work to deepen philanthropic partnerships in the county and build new ones. Passionate volunteers and donors have helped fuel City of Hope’s ability to deliver exceptional, compassionate care for more than a century. This support will be vital in helping City of Hope extend its powerful capabilities to improve the health and well-being of Orange County residents.

City of Hope Orange County will be anchored by an existing 190,000-square-foot building.



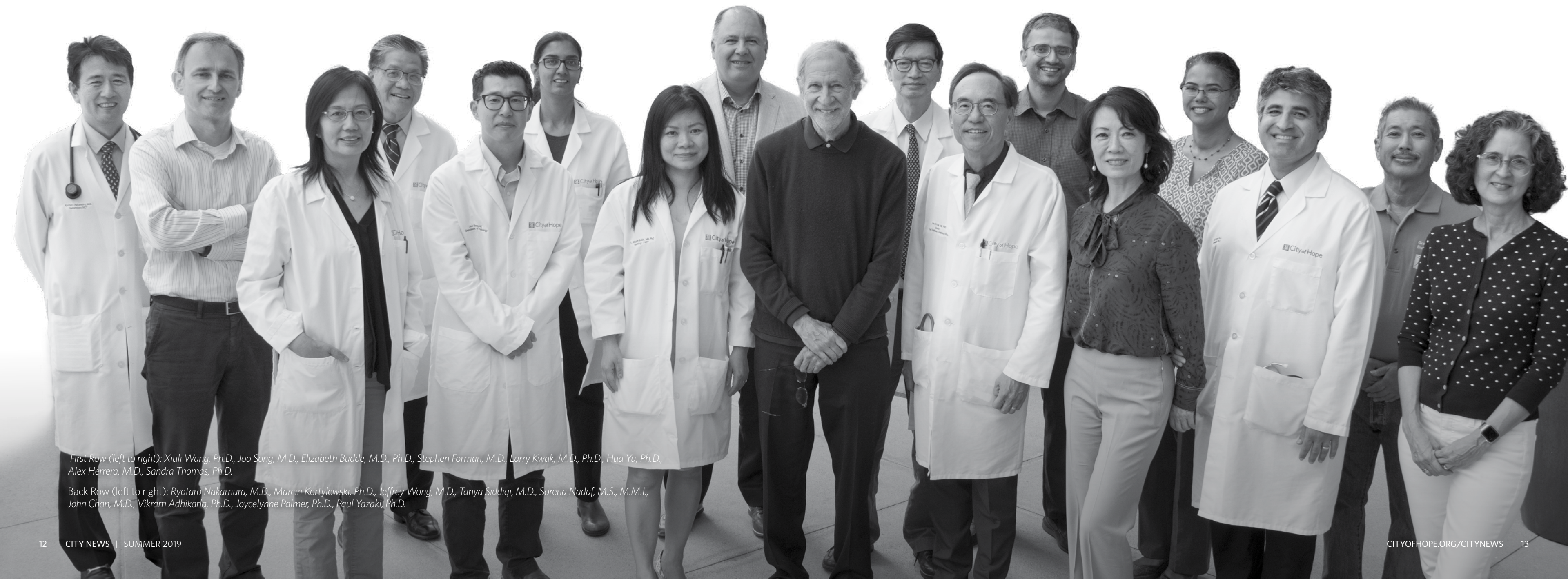
The Team to Beat

With a vast team and new NCI funding,
City of Hope takes on lymphoma

BY LETISIA MARQUEZ

An international leader in finding innovative treatments for lymphoma patients, City of Hope has earned its third Lymphoma Specialized Programs of Research Excellence (SPORE) grant from the National Cancer Institute (NCI), one of just four current NCI-supported lymphoma SPOREs in the nation.

The grant covers a five-year period and totals \$12.5 million.



First Row (left to right): Xiuli Wang, Ph.D., Joo Song, M.D., Elizabeth Budde, M.D., Ph.D., Stephen Forman, M.D., Larry Kwak, M.D., Ph.D., Hua Yu, Ph.D., Alex Herrera, M.D., Sandra Thomas, Ph.D.

Back Row (left to right): Ryotaro Nakamura, M.D., Marcin Kortylewski, Ph.D., Jeffrey Wong, M.D., Tanya Siddiqi, M.D., Sorena Nadaf, M.S., M.M.I., John Chan, M.D., Vikram Adhikarla, Ph.D., Joycelynne Palmer, Ph.D., Paul Yazaki, Ph.D.

SPORES — a cornerstone of the NCI's efforts to promote collaborative, interdisciplinary translational cancer research — involve both basic and clinical/applied scientists working together to support projects that will result in new and diverse approaches to the prevention, early detection, diagnosis and treatment of cancer. City of Hope's interdisciplinary lymphoma research is currently advanced in the Toni Stephenson Lymphoma Center, which is part of City of Hope's Hematologic Malignancies and Stem Cell Transplantation Institute.

"City of Hope is developing novel therapeutics and prognostics representing the forefront of knowledge gained from observations in molecular biology and cellular immunology here," said Larry W. Kwak, M.D., Ph.D., vice president and deputy director of City of Hope's comprehensive cancer center, director of the Toni Stephenson Lymphoma Center and the Dr. Michael Friedman Professor in Translational Medicine. "Six clinical trials are proposed in this grant, five of which utilize agents (cellular products, small molecules, radiolabeled antibodies) that will be produced at City of Hope in its GMP Manufacturing Core and have been developed from the institution's preclinical laboratory studies."

The SPORE grant is led by Stephen J. Forman, M.D., the Francis & Kathleen McNamara Distinguished Chair in Hematology and Hematopoietic Cell Transplantation, and Kwak as principal investigators. This is the 11th year City of Hope has received funding from the NCI for a lymphoma SPORE grant.

Over the next five years, City of Hope doctors and researchers, as well as scientists from other institutions, will focus on the following projects for the SPORE grant:

A KILLER COMBO FOR NON-HODGKIN'S LYMPHOMA

After patients with non-Hodgkin's lymphoma have received a blood stem cell transplant with their own stem cells or those of a donor, there could still be enough cancerous cells not killed by the procedure for the disease to recur. A treatment option for these patients is combining a transplant with chimeric antigen receptor (CAR) T cell therapy. The therapy works by taking a person's immune cells — T cells — and adding a CAR that helps target and wipe out cancerous cells. The institution is now looking for ways to improve the treatment.

One option that will be tested is adding CD19-specific CAR, which targets the CD19 protein in cancerous B cells, to a virus-specific T cell that can be stimulated to multiply using a vaccine. City of Hope researchers plan to add the Triplex vaccine — developed here — to the CAR T cells. Triplex already has been shown to be safe in a City of Hope phase 2 trial in transplant patients. Because Triplex can stimulate T cells to multiply, researchers hope that the vaccine will boost the number and longevity of CMV-CD 19 CAR T cells in these trials in patients' bodies so they may better fight against their disease.

2 TRIALS FOR RELAPSED/RESISTANT HODGKIN'S

Patients with high-risk Hodgkin's lymphoma who have relapsed or resisted treatment currently only have a 20 to 50% chance of achieving a cure.



The Toni Stephenson Lymphoma Center is housed in Beckman Research Institute of City of Hope

City of Hope is leading two compatible clinical trials for these patients; the therapies are expected to treat the disease, which would then enable them to receive a bone marrow transplant. Led by Alex Herrera, M.D., City of Hope assistant professor in the Department of Hematology & Hematopoietic Cell Transplantation, the first is a phase 2 trial of response-adapted sequential therapy using a combination therapy — nivolumab, an immunotherapy drug known as a PD-1 inhibitor, and ICE (ifosfamide, carboplatin, etoposide phosphate) chemotherapy.

A second aim of the project, led by Eileen Smith, M.D., City of Hope associate director of the Clinical Research Program, Department of Hematology & Hematopoietic Cell Transplantation, is to start a phase 2 trial that uses an anti-CD25 antibody immunoconjugate, a targeted therapy that uses a CD25 antigen to kill tumor cells.

FIGHTING STAT3 IN NON-HODGKIN'S LYMPHOMA

Non-Hodgkin's lymphoma is the sixth most common cancer in the United States, with more than 74,000 estimated new cases each year. Growing evidence links B cell non-Hodgkin's lymphoma to persistent activation of STAT3, a gene that drives tumor cell growth and anti-tumor immune suppression. But there is currently no drug approved by the U.S. Food and Drug Administration that stops the activation of STAT3. Hua Yu, Ph.D., City of Hope's Billy and Audrey L. Wilder Professor in Tumor Immunotherapy and co-leader of the Cancer Immunotherapeutics Program, and Marcin Kortylewski, Ph.D., associate professor, Department of Immuno-Oncology, and team have already demonstrated that an immunotherapy developed at City of Hope (CpG-STAT3siRNA) turns off STAT3 and stimulates the immune system to attack tumors, in addition to killing B cell lymphoma tumor cells and making radiation therapy more effective in animal models.

The new lymphoma SPORE grant — as well as funding from The Marcus Foundation — makes it possible for City of Hope to start a phase 1 trial for that drug in patients. The trial will test its safety in patients, and whether the therapy can be injected into tumors.

PREDICTING AUTOLOGOUS STEM CELL TRANSPLANT RISKS

Hodgkin's lymphoma (and non-Hodgkin's lymphoma) patients who receive stem cell transplantation can develop a deadly complication that may arise after the procedure. Between 6 to 8% of these transplant patients can develop therapy-related myelodysplasia/acute myeloid leukemia (t-MDS/

AML), which is more common in older adults and is the leading cause of nonrelapse mortality in this group. It is generally believed that blood stem cells exposed to high doses of chemotherapy and other cytotoxic therapies suffer genetic damage that leads to t-MDS/AML, but some patients could also have a genetic predisposition to the disease.

Researchers at University of Alabama Birmingham, City of Hope, University of Minnesota, University of Nebraska, St. Jude Children's Research Hospital and Dana Farber Cancer Institute are developing a prediction model that includes clinical and genetic details to determine the probability of a patient developing t-MDS/AML. The research will help identify which patients are at risk and what a medical team can do to personalize treatment and help prevent a patient from developing the disease.

Stephenson Gift Lays the Foundation for City of Hope's Continued Success With SPORE Grants

The support of donors Emmet and Toni Stephenson and their daughter Tessa Stephenson Brand through the Toni Stephenson Lymphoma Center has helped to create the collaborative, fast-paced culture in which the projects in the new Lymphoma Specialized Programs of Research Excellence (SPORE) grant will be advanced. The Toni Stephenson Lymphoma Center has attracted the best and the brightest researchers in the blood cancer field, including Larry W. Kwak, M.D., Ph.D., who directs the center and is also vice president and deputy director of City of Hope's comprehensive cancer center. Kwak, the Dr. Michael Friedman Professor in Translational Medicine, is one of the investigators leading the SPORE grant along with Stephen J. Forman, M.D., the Francis & Kathleen McNamara Distinguished Chair in Hematology and Hematopoietic Cell Transplantation. Kwak was also recently appointed the deputy director of the Hematologic Malignancies and Stem Cell Transplantation Institute.

Researchers at the Toni Stephenson Lymphoma Center are driving life-giving discoveries and developing unique combinations of therapies, with a special focus on rare and aggressive forms of the disease, including T cell lymphoma. The number of patients enrolled in clinical trials has been growing every year.

Emmet and Toni Stephenson are engaged not only in philanthropy to establish the center, but are full partners in accelerating lymphoma research and enhancing all aspects of patient care. Their leadership has been integral in helping City of Hope build on its strength of integrating scientific findings and superior treatment to create an expanded effort for blood cancers and fulfill its strategic mission.

Now in remission, Toni Stephenson herself was a patient in a clinical trial supported by SPORE funding. The Stephensons' investment in lymphoma research, treatments and care ensures that the virtuous cycle of treatment innovation supported by SPORE funding continues at City of Hope.

Three generations of the Stephenson family





An Engineer Tackles a Cancer Challenge

BY MAXINE NUNES

How math is key to developing the perfect CAR T therapy

What's an engineer who worked in aerospace and robotics doing at City of Hope? Exploring what may be the final frontier of cancer research.

Vanessa Jonsson, Ph.D., has solved tough problems for the Aquarius Mission at NASA's Jet Propulsion Laboratory and helped design autonomous cars for the Defense Department's DARPA program.

But she also had an avid interest in medicine, and received her doctorate in engineering with a specialization in biology. Armed with this unique set of skills, she has already made valuable contributions to medical research at Caltech and University of California San Francisco.

"My real passion was always to work on cancer," she said. "Then I had this wonderful opportunity to work on immunotherapies at City of Hope."

Jonsson is now an assistant research professor and group leader in computational immuno-oncology at Beckman Research Institute of City of Hope. Her team focuses on chimeric antigen receptor (CAR) T cell therapy, an immunotherapy that uses a patient's own T cells — the cells in our bloodstream that ward off disease — to fight cancer.

With this exciting new technology, T cells are extracted from the patient and engineered to destroy a tumor by recognizing its antigen — a protein that stimulates an immune response. The T cells are then multiplied in the lab and transfused back into the patient.

SEVERAL ADVANTAGES

The advantages of CAR T over traditional therapies are impressive. The CAR T cells attack only the tumor, not healthy tissue, and have a long lifespan in the bloodstream. What's more, in addition to targeting specific antigens, CAR T therapy may also be able to boost the way the rest of a patient's immune system responds to cancer.

"If you can simultaneously target cancer cells and amplify a patient's own immune response, you have a very powerful therapy. That's the hope with CAR T cell therapy," said Jonsson.

There is, however, more to be learned about CAR T therapy. While it appears to be quite effective for some blood cancers, with solid tumors like brain, breast, lung and colon cancers, the issue is more complicated, and tumors are still likely to return.

Jonsson explained the crux of the problem: "The tumor is 'smart' enough to evolve away from these therapies," she said. For example, it can express new antigens that are different from those the CAR T cells were engineered to attack, or hide itself from the immune system.

Her job is to outsmart the tumor, and she comes well prepared for the fight.

Using such tools as computational analysis and mathematical modeling, she examines the complex

interactions between the tumor, the patient's immune system and the therapy to learn just how the tumor evades the immune response.

"We are studying the ways in which tumors can become resistant to immunotherapy and then, using engineering techniques, optimize the way we treat patients effectively by combining different therapies," she said.

She recently conceived of and developed an algorithm to fight tumor regrowth in the context of lung cancer — and the results look promising.

"We found that combinations of two targeted therapies couldn't do the trick. So we designed a switching strategy — starting off with one targeted drug combination, and after some time switching to another to box in the evolution of the tumor," she said.

DOING THE MATH

In the laboratory, her algorithm succeeded in predicting the optimal strategies for outsmarting lung cancer tumors in vitro. The findings were published in Scientific Reports last year.

She'll now take that work to the next level, heading up data analytics for several of City of Hope's CAR T trials: for glioblastoma (the most common type of brain cancer), prostate cancer, metastatic breast cancer and multiple myeloma.

Jonsson's combination of engineering and medical research skills reflects two of her lifelong passions. As a kid, she'd always been interested in math and science, but when she was 16, she volunteered at a private hospital. There she had a chance to observe meetings in which physicians brainstormed ways to better treat patients with complicated cases.

"That was the part that really fascinated me: getting to the bottom of a medical mystery," she said.

It's this process of discovery and problem-solving that drives her work. It's also what she finds most exciting about her new position at City of Hope.

"The great thing about City of Hope is that there's such a tight relationship between the clinical and research side. As a researcher, I can attend clinical meetings, discuss research results with clinicians and other scientists, and be in a place where I can eventually see my research affect patients in a positive way," she said. "It's an exciting opportunity to be part of this highly collaborative, multidisciplinary team."

But there's more to this scientist than algorithms and analysis. Jonsson also loves the arts. She's a trained violinist who once played professionally, and when she's not at work, you might find her taking photos on the streets of Los Angeles — downtown, the Arts District, Olvera Street. "I'm really interested in capturing personal stories through photography," she said.

Vanessa Jonsson, Ph.D.



Guitar HERO

*Def Leppard
Guitarist
Defies
Cancer
Diagnosis*

BY SAMANTHA BONAR

Photo by Kevin Nixon

Cancer has no respect for nasty guitar licks. More than 8,000 people are diagnosed with Hodgkin's lymphoma in the United States each year, and in 2013, Def Leppard guitarist Vivian Campbell was one of them. (Def Leppard was inducted into the Rock & Roll Hall of Fame on March 29.)

During a career spanning four decades, Campbell has performed with such groups as Thin Lizzy, Dio, Whitesnake and Lou Gramm. The Ireland native joined Def Leppard in 1992.

At age 50, Campbell had been suffering from fatigue, intermittent fever, night sweats and a nagging cough for almost a year while touring with the band. He'd visited doctors multiple times and downed several courses of antibiotics. But he couldn't shake his "infection."

Finally, his doctor ordered a chest X-ray. A CT scan and lymph node biopsy followed in quick succession, and Campbell was confronted with the shocking diagnosis: Stage 2b Hodgkin's lymphoma.

Hodgkin's lymphoma occurs mainly in individuals between 16 and 34 years of age and those over age 55. Lymphoma is a general term for cancers that develop in the lymph system, part of the body's immune system. Hodgkin's lymphoma is a type of lymphoma that develops in the white blood cells. While it can start in the lymph nodes, it can spread to almost any organ or tissue, including the liver, bone marrow and spleen.

Originally treated by an oncologist in Santa Monica, California, Campbell underwent six months of chemotherapy. Unfortunately, within a few months of finishing treatment, signs of cancer returned. At that point he was referred to Stephen Forman, M.D., the Francis & Kathleen McNamara Distinguished Chair in Hematology and Hematopoietic Cell Transplantation at City of Hope.

A HEAVY LOSS

Forman placed him on a tough chemotherapy regimen in preparation for an autologous stem cell transplant. "All this time I was still working. I was still touring with Def Leppard," Campbell recalled. "I started the tour with hair, and I ended up with no hair and no eyebrows." For a heavy metal guitarist, losing his long hair made him feel vulnerable and exposed. However, "It really made me focus on my performance as a musician, as a singer and a guitar player. It really helped me look inward to that, and to focus on that. I couldn't go out there and pretend to be a rock star. I was a cancer patient. It was liberating in a way," he said. He bought a wig but never wore it, deciding instead to "rock" the bald look.

In October 2014, Campbell underwent his stem cell transplant, which "didn't work either." Within a few months, the cancer was back. The next suggested step was radiation, but Campbell

was resistant. He asked Forman about a new immunotherapy drug he'd read about called pembrolizumab (Keytruda). Forman jumped on board, suggesting he join a clinical trial of pembrolizumab being coordinated by Alex Herrera, M.D., an assistant professor in the Department of Hematology & Hematopoietic Cell Transplantation at City of Hope. Campbell began pembrolizumab infusions in 2015.

The U.S. Food and Drug Administration granted accelerated approval to pembrolizumab in March 2017 for treatment of Hodgkin's lymphoma. The approval came after a clinical trial found that 22% of patients who were treated with pembrolizumab underwent complete remission.

'NO SIDE EFFECTS'

"Compared to chemo, it's so, so easy," Campbell said. "I've had practically no side effects. The hardest part of it for me to this day continues to be the scheduling because I travel so much for work." Campbell receives pembrolizumab infusions roughly once a month. Although pembrolizumab causes an average remission of up to 24 months, the medication has held his cancer at bay for almost four years.

"He is doing extremely well, in large part due to modern innovations in immune-based therapy as a treatment for cancer," Forman said.

"I consider myself very, very fortunate that I've been able to find this treatment that I've responded to so well," Campbell said. "Being able to continue my life and continue my work, I think, has been a big part of being able to come through all of this. My work is what keeps me alive. My bandmates initially wanted me to stay home and convalesce. I'm stubborn and I'm Irish and I never wanted to do that. I've always refused to capitulate to the cancer. I just wanted to give cancer the big middle finger and go on."

Forman's plan is to keep Campbell on the pembrolizumab as long as it is working or until something better comes along. That is fine with Campbell. He feels well and his outlook is positive.

"I've always been a glass half-full kind of person, but now with cancer, my glass is brimming," he said. "You really kind of recalibrate your thinking about each and every day in life. You look at your life a different way and you look at your priorities a different way. It helped me become a better guitar player. It helped me look inward.... It's just been good for me. I kind of always look at it as when life gives you these sorts of obstacles, you have two choices. You can give in or you can fight, you know?"



welcome to the ROBOTIC SURGERY revolution

BY ABE ROSENBERG

Yuman Fong, M.D., robotic surgery pioneer

In the three decades since robots first entered the operating room, these increasingly sophisticated machines have helped surgeons perform more than a million procedures, all over the human body: Bypassing a clogged artery. Removing a gall bladder. Replacing a hip. Removing liver tumors. And more.

For a growing number of cancer surgeons at City of Hope, robotic surgery is rapidly becoming the new normal. Well over 12,000 robotic procedures have taken place here, and the trend is clear.

"In terms of clinical as well as public acceptance," said Yuman Fong, M.D., The Sangiacomo Family Chair in Surgical Oncology and chair of the Department of Surgery, "robotic surgery is no longer experimental. It's routine."

So routine, in fact, that some surgeons now perform most of their procedures robotically, and more clinicians are joining them.

As a result, more patients than ever can be "cured," even while they spend less time than ever in the hospital.

Take liver surgery," said Fong. "It used to require at least a day in intensive care, a total of seven to 10 days' hospitalization. With robotics, half our patients go home in 24 to 36 hours. It's practically an outpatient procedure."

Similar progress is evident in other areas.

"Five years ago," said Fong, "you couldn't even attempt esophageal surgery robotically. They sneered at you. Now it's the way we do most esophageal procedures. Using robotics for thyroid cancer was impossible five years ago. Now we have three different methods for doing it."



IMPROVING TECHNOLOGY

Fong's colleagues echo his enthusiasm.

"We are doing much more complex surgery for kidney cancer," said urologist Bertram Yuh, M.D. "[For many] patients who previously would have had their entire kidney removed, we are sparing most of their kidney, even with larger tumors."

RISE OF THE ROBOTS

"We are now at a pivotal point in the field," Fong recently wrote, "when a technology is about to transform from a tool for innovators and experts to a tool for general practitioners."

Robotic technology builds upon the considerable benefits of minimally invasive, manually performed laparoscopic surgery. Laparoscopy makes tiny incisions, which means less trauma, less blood loss, fewer or even no sutures (often a Band-Aid will do), much less pain and faster recoveries.

The latest robotic machines add an astounding level of precision. 3D video screens enable surgeons to see more (even around corners), while ultra-miniature instruments are guided to remove the smallest, most awkwardly located tumors no human hand could ever reach.

"In the past eight years of my practice," said Yanghee Woo, M.D., a stomach cancer specialist, "I have performed over 200 robotic surgery operations ... approximately 70% of my gastric cancer operations performed for curative intent are using the robotic surgical platform."

NEW PLAYERS IN THE MARKET

The platform is expensive. A robotic machine can cost upward of \$2 million, and robotics can add thousands of dollars to the cost of an operation. Competition is expected to bring costs down.

One recently approved technology makes no external incisions at all. Another company is marrying robotics and artificial intelligence, with an eye toward automating many surgical procedures. This may be the most exciting development of all.

KUO GIFT SPEEDS THE WORK OF FONG'S LIVER CANCER TEAM



Samuel Kuo and Grace Liu

The pioneering work of Yuman Fong, M.D., is a fitting target for the generosity of Samson Holding, Ltd, Samuel Kuo and Grace Liu, who recently gave \$2 million to further Fong's work with liver cancer. In addition to his expertise with the newest robotic surgical techniques, Fong leads a group of doctors and researchers whose work is at the forefront of the way liver cancer is being treated worldwide.

Kuo and Liu are themselves pioneers, responsible for several innovations in furniture manufacturing that helped establish Samson Holding as a leader in the global furniture business. They were the first to open a furniture-manufacturing facility in China, and their development of new container shipping methods opened the door for small and medium U.S. retailers to import furniture directly from Asia. Today Samson Holding is the parent company of many U.S. and international furniture brands, with a presence in China, the U.S., Bangladesh and Indonesia.

Samson Holding, Kuo and Liu have supported City of Hope for nearly 20 years. They were recognized with The *Spirit of Life*® Award in 2018 for their personal, professional and philanthropic achievements.

Kuo and Liu see urgency in the need to fight liver cancer, given that it is the second-leading cause of cancer death in men globally and the sixth-leading cause of death in women, according to the American Cancer Society. Incidence rates of liver cancer are especially high in the Southeast Asia region, as well as parts of Africa.

The generous gift of Samson, Kuo and Liu in support of Fong's lab is a natural extension of their global vision, as they are supporting work at City of Hope that has the potential to change the way liver cancer is treated around the world.

Considering the CAREGIVERS

BY MAXINE NUNES

City of Hope researchers have just received a \$2 million grant from the National Cancer Institute to study a crucial but rarely examined aspect of patient care and quality of life: the family caregiver.

The study was designed by principal investigators Virginia Sun, Ph.D., R.N., M.S.N., associate professor, Division of Nursing Research and Education, and Jae Kim, M.D., associate professor and chief of the Division of Thoracic Surgery.

“Family caregivers have been left out in many ways, and we really need to understand how to take better care of them,” Sun said.

The term “family caregiver,” she explained, includes any nonprofessional friend or significant other who is the primary caregiver for a patient.

Many of the problems caregivers face — among them high levels of stress and lack of preparation for the tasks they must perform — were documented in the 2016 report “Cancer Caregiving in the U.S.”

Sun and Kim conceived the study after the eye-opening results of a previous trial they had worked on. It revealed that while standard intervention and education methods were helpful for patients — they were not so helpful for their caregivers.

“This was particularly true for surgery,” said Sun. “The quality of life for patients rebounds relatively quickly — but it takes a longer time for caregivers to recover.”

That’s why, for this study, they will focus exclusively on lung cancer surgery, Kim’s area of expertise.

SURGICAL ADVANCES MEAN A GREATER NEED FOR FAMILY CAREGIVERS

With technological advances and an increase in minimally invasive surgery, there’s often no need for long hospital stays.

“In fact, it’s better for most patients to go home,” said Kim. “It helps them recover and resume their normal lives faster.”

However, when caregiver preparation isn’t adequate, the patient may wind up in urgent care, an emergency room or even a nursing facility, where a long stay can lead to complications.

Kim has seen this too often. Recently, one of his patients contracted a serious infection in a nursing facility and had to be readmitted to the hospital.

“I’m convinced that if her husband had been better prepared to take care of her, and if we had given him the resources he needed to be psychologically and emotionally prepared for caregiving, I don’t think that complication would have happened,” he said.

What’s more, though there’s insufficient data for a direct cause-and-effect link, when caregivers fall ill themselves, the stress of caregiving may sometimes be the cause.

THE STUDY’S INNOVATIVE APPROACH

Caregiver preparation has often consisted of videos and print materials developed by groups like the American Cancer Society. They’re informative — but Sun and Kim realized that wasn’t enough. They had to think about the problem in a different way.

It’s not that helpful to just give information, Sun said. “We need tools that can help caregivers self-manage the individual issues that come up for them.”

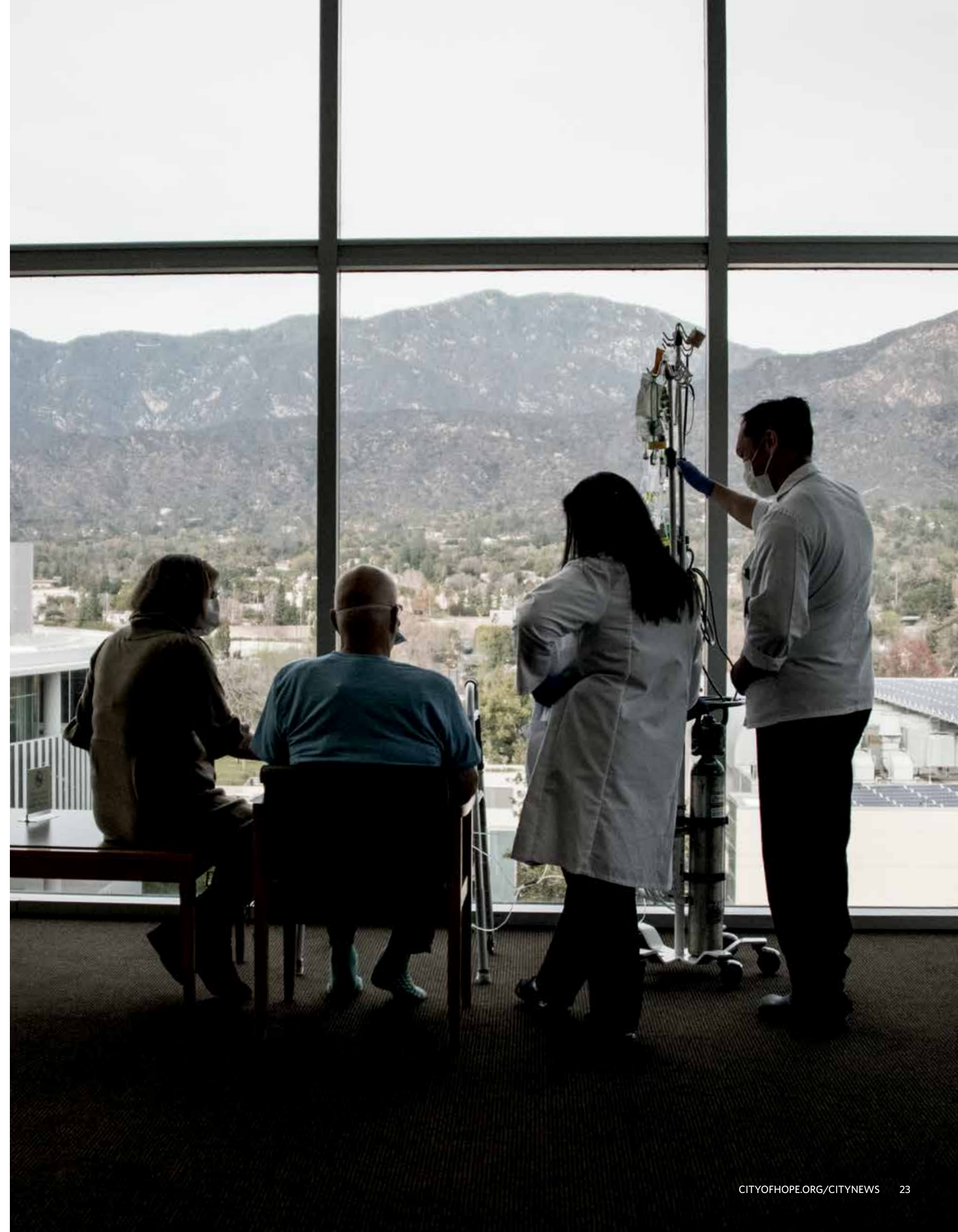
Over the course of five years, the pair plan to recruit 160 patient/caregiver dyads. The intervention will begin when the decision to have surgery is made and continue for 90 days after the patient’s hospital release.

In this randomized trial, the control arm will receive the standard ACS material. The intervention arm will be given video and print material developed for the study, specifically for lung cancer surgery patients and caregivers. In addition, there will be face-to-face sessions with a nurse to help deal with specific needs and problems.

Sun and Kim will be working with co-investigators Dan Raz, M.D., M.A.S., assistant professor and co-director, Lung Cancer and Thoracic Oncology Program; Loretta Erhunmwunsee, M.D., assistant professor, Division of Thoracic Surgery; and Betty Ferrell, Ph.D., M.A., R.N., director and professor, Division of Nursing Research and Education.

“Our hope,” said Sun, “is that this nurse-led intervention will have a positive impact on both caregivers and patients, creating better outcomes for both.”

Supportive Care Medicine staff with a patient and his family caregiver



New Gene Linkage Sheds Light on Common Liver Cancer

The incidence of hepatocellular carcinoma (HCC), the most common form of liver cancer, has nearly doubled over the last decade, making it the fastest growing type of cancer in the U.S. and the third-leading cause of cancer-related death worldwide.

In an article published April 5 in the scientific journal *Cancers*, two researchers at the Translational Genomics Research Institute (TGen), an affiliate of City of Hope, provide the first summary of the experimental evidence supporting the AKR1B10 enzyme as a promising therapeutic target for HCC, based on a review of more than 50 studies published since this gene was first identified and characterized in 1998.

“While the association between this gene and HCC is well recognized, in this review we see AKR1B10 emerging as not only a therapeutic target for this type of liver cancer, but also having potential use in early diagnosis of this deadly disease,” said Johanna DiStefano, Ph.D., head of the Diabetes and Fibrotic Disease Unit at TGen.

Importantly, AKR1B10 has a seemingly conflicting role in HCC development and progression. This gene’s overexpression is a clear indicator that a patient might have HCC, and yet the suppression of this gene may also be seen as a way to stop the cancer’s progression and spread, said DiStefano, a professor at TGen and the paper’s senior author.

Like many types of digestive cancers, HCC exhibits few symptoms in its early stages, and is usually not diagnosed until its late stages, when there are fewer options for treatment and the chances of patient survival are slim.

In the U.S., the number of liver cancer diagnoses has nearly doubled, from about 22,000 cases in 2009 to an estimated 42,000 cases this year. Men are almost twice as likely to contract this disease as women.

This year, nearly 32,000 patients will die of liver cancer, making it the fifth leading cause of cancer-related death in the U.S., following closely

on the heels of breast and pancreatic cancers. Worldwide, liver cancer is the third leading cause of cancer-related death, according to the review paper “Diagnostic and Prognostic Potential of AKR1B10 in Human Hepatocellular Carcinoma.”

HCC is the most common cause of death in patients with cirrhosis of the liver, which is most strongly associated with overconsumption of alcohol, viral infections and nonalcoholic fatty liver disease.

While AKR1B10 has emerged as a potential biomarker for the diagnosis and prognosis of HCC, studies show this enzyme also plays a role in the development and progression of HCC, the paper says. AKR1B10 appears to affect HCC’s resistance to currently available chemotherapies, making

“This year, nearly 32,000 patients will die of liver cancer, making it the fifth leading cause of cancer-related death in the U.S.”

HCC more difficult to treat. At the same time, the TGen paper shows that higher expression of this gene is paradoxically associated with better long-term outcomes, increased survival rates and lower incidence of metastatic spread to other parts of the body. The aggregate findings suggest that AKR1B10 may be performing different functions at different stages of HCC.

“Identification of biomarkers for various stages of HCC is critical to improving early disease detection and enabling early

implementation of chemotherapy and surgical removal of the tumor to prevent the cancer’s progression and spread to other organs,” said Bethany Davis, a postdoctoral fellow in DiStefano’s lab and co-author of the paper.

The molecular mechanisms underlying HCC, and the role AKR1B10 plays in this disease, however, continue to remain poorly understood, DiStefano said.

“Still, our review shows that AKR1B10 might be exploited for early cancer prevention,” she said. “And the value of this gene in therapies and clinical management of specific subtypes of HCC clearly warrant further investigation.”

Roberts Fellowship Has Lasting Impact on Liver Cancer Research

When Natalie Roberts lost her husband David to liver cancer, she decided to do something about it. She approached City of Hope about a gift in his memory aimed at providing diagnosis sooner, and treating liver cancer more powerfully. In 2017, the Natalie and David Roberts Fellowship in Liver Cancer was created to attract new and emerging talent in cancer research to City of Hope. As part of their experience, Roberts fellows receive mentoring and support from City of Hope physician-researchers who are at the top of this field: Yuman Fong, M.D., The Sangiacomo Family Chair in Surgical Oncology, and Susanne Warner, M.D.

Natalie Roberts and her family have long-standing connections with City of Hope that made the decision to partner on philanthropic projects a natural one. She and her husband made City of Hope a regular part of their charitable giving, and this tradition is continuing today.

The Roberts Fellowship is an endowed fund, ensuring lasting impact on liver cancer research at City of Hope by the Roberts family.



Finding *and* Treating Cancer *at the Same Time*

A new type of therapy allows doctors to identify
and treat cancer all at once

BY ZEN VUONG

Ammar Chaudhry, M.D.

City of Hope scientist and his colleagues have developed a user-friendly approach to creating “theranostics” — therapy combined with diagnostics — that target specific tumors and diseases.

Key to the process are molecules called metallocorroles, which serve as versatile platforms for the development of drugs and imaging agents. Metallocorroles both locate (via imaging) and kill tumors. City of Hope’s John Termini, Ph.D., and his colleagues at Caltech and the Israel Institute of Technology have developed a novel method to prepare cell-penetrating nanoparticles called “metallocorrole/protein nanoparticles.” The theranostics could both survive longer in the body and better snipe disease targets.

“This study is just one of City of Hope’s many ongoing research projects that aim to move the field from conventional medicine to precision medicine, where therapies are tailored for specific individuals,” said Termini, a molecular medicine professor at City of Hope.

The study, published in *Scientific Reports*, a *Nature* publication, on Feb. 19, details a unique way the researchers prepared the theranostics that may be generalizable to many similar molecules.

“While corroles have shown great promise in this application, directing them specifically to cellular and tissue targets, e.g., the brain, was an unsolved technical problem,” Termini said. “This manuscript describes and characterizes a general approach for preparing protein nanoparticles where the protein ‘coat’ directs the encapsulated corrole to specific targets such as breast cancers or tumors in the brain for imaging and therapy applications.

“Through collaborative brainpower, we were able to create something that has huge chemotherapeutic potential,” Termini said. “Down the road, theranostics such as this could shorten treatment duration and diminish the dreaded side effects so many cancer patients fear.”

USING IMAGING TO ASSESS TUMORS WITHOUT BIOPSY

Termini’s work is similar to that being done by Ammar Chaudhry, M.D., founder and director of City of Hope’s Precision Imaging Lab and one of the

Chaudhry has developed a noninvasive technology to assess not just a few tumors, but every cancer site throughout the body.

Barron Scholars Program Unites Talent Across the Globe in the Fight Against Cancer

Strengthening international collaboration to advance cancer research and treatment was exactly what Harvey Miller had in mind when he made a generous gift through his family’s foundation in 2016 to establish the Jacki and Bruce Barron Cancer Research Scholars’ Program. As a partnership between City of Hope and the Israel Cancer Research Fund, this program fosters innovative collaborative research and promotes the exchange of ideas among researchers in the United States and Israel.

The program focuses on advancing scientists’ understanding of cancer and the development of lifesaving therapies, novel diagnostic approaches and prevention strategies by leveraging the knowledge, expertise and resources in the two countries.

A longtime supporter of City of Hope from his days as a leader in the business products industry, Miller recognized that bringing like-minded investigators together would help expedite answers to complex questions of prevention, diagnosis and treatment. Now in its third year, the Barron Program awards grants to City of Hope and Israeli scientists to support basic, translational and clinical research.



Barron Scholars Jeffrey Weitzel, M.D., the Dr. Norman & Melinda Payson Professor in Medical Oncology and director of the Division of Clinical Cancer Genomics at City of Hope, and his partner Gad Rennert, Ph.D., professor and chairman of the Department of Community Medicine and Epidemiology at the Carmel Medical Center and B. Rappaport Faculty of Medicine at the Technion-Israel Institute of Technology, are working to determine the genetic mutations most significantly associated with increased risk of breast cancer in young women beyond the well-known genes BRCA1 and BRCA2.

Shai Izraeli, M.D., is the Dora and Gregorio Shapiro Chair of Hematological Malignancies, Tel Aviv University, and research professor, Department of Systems Biology, City of Hope. In 2016, Izraeli partnered with Hua Yu, Ph.D., the Billy and Audrey L. Wilder Professor in Tumor Immunotherapy at Beckman Research Institute of City of Hope, on new therapeutic approaches to acute lymphoblastic leukemia in adults. In 2018, he worked with Markus Müschen, M.D., Ph.D., The Norman and Sadie Lee Foundation Professor in Pediatrics and chair, Department of Systems Biology, City of Hope, to improve the targeting of cancer stem cells in patients with B cell leukemia, the most frequent type of cancer in children and young adults.

City of Hope’s John Termini, Ph.D., professor in the Department of Molecular Medicine, his colleagues at Caltech and his colleague Zeev Gross, Ph.D., of the Israel Institute of Technology, have developed a user-friendly approach to therapy combined with diagnostics (theranostics) that targets specific tumors and diseases. Their research is an example of how these partnerships aim to move the field from conventional medicine to precision medicine, where therapies are tailored to specific individuals.

Continued next page.

first recipients of the new ORIEN NOVA Award. The \$1 million grant will fund research for his breakthrough approach to cancer imaging and diagnosis. Chaudhry’s study will focus on a major challenge in this era of targeted cancer therapies — creating advanced diagnostic technologies to help fully realize the potential of these remarkable new treatments.

“The new immunotherapies have been extremely effective for some patients, but the results have been mixed in others,” Chaudhry said. “And the key to better prediction lies in more accurate diagnosis for patient selection.”

He will be working with David Carbone, M.D., of The Ohio State University, an internationally renowned lung cancer specialist.

Chaudhry has developed a noninvasive technology to assess not just a few tumors, but every cancer site throughout the body. The results should be applicable for many different types of treatment, but this study will focus on one medication, pembrolizumab, an immune checkpoint inhibitor that has been Food and Drug Administration-

“Theranostics ...
could shorten
treatment duration
and diminish the
dreaded side effects
so many cancer
patients fear.”

John Termini, Ph.D.

approved for lung cancer, melanoma and several other types of cancer.

“Basically, we bind the imaging agent copper-64 to pembrolizumab, then we inject it through an IV, which takes about a minute,” Chaudhry explained. “Twenty-four hours later, we do a whole-body PET-

CT scan to see where the imaging agent lights up. If it has been taken up at the cancer sites, the patient should respond to immunotherapy treatment.”

GENOMIC ANALYSIS

The unusually large grant and the small size of this two-year study — they plan to enroll just 20 patients — will allow greater depth than most pilot projects, and in addition to imaging, they will also do a genomic analysis of the subjects.

Chaudhry decided on this aspect of the study when he noticed that certain mutations increase or decrease the expression of PDL1, a protein marker in tumors that responds to pembrolizumab. Patients with a mutation that suppresses PDL1 aren’t good candidates for this drug — but the genomic information can open the door to alternative treatments.

“I don’t just want to tell the patient, ‘Sorry, you’re not going to respond to pembrolizumab,’” he said. “With a genomic assessment, I can suggest another therapy they’re more likely to respond to. After all, we’re at City of Hope and I want to give them hope.”

Marilyn Wallace and Sami Freedman:
A Shared Passion for Curing Cancer

Sisters Marilyn Wallace and Sami Freedman, originally from Omaha, Nebraska, were raised in San Francisco and moved to Los Angeles in 1966. The two share a lot of passions, but what they value most is the gift of their close relationship with each other.

“Sami and I are like one person in two bodies,” shared Marilyn, “and we are much alike in many ways, and very different in many ways.” They also share a passion for helping others and finding a cure for cancer.

Marilyn and Sami’s family connections to City of Hope reach back decades; both their uncle as well as Marilyn’s father-in-law received treatment at City of Hope.

Their interest deepened through their friendships with committed City of Hope supporters Shirley and Isadore (Izzy) Familian. As a City of Hope board member for many years, Izzy continually shared his enthusiasm and support for City of Hope’s work. His passion inspired Marilyn and Sami, who said, “I think he would be very proud to see our involvement now.”

In 2017, their friends Stephan and Linda Tow brought them to visit City of Hope. Later, they met Steven T. Rosen, M.D., provost and chief scientific officer, and the Irell & Manella Cancer Center Director’s Distinguished Chair, and they felt an immediate connection with him as he shared his scientific vision for the institution.

“Their work reaches beyond California — it will help people all over the world,” said Marilyn. The sisters have established the Rosinsky, Silver, Wallace, Freedman Innovator Endowed Fund through their estate plans, with the goal of advancing cancer research by accelerating early-stage research into clinical trials that will create more novel therapies and save lives.



“Neither of us have children, so this will be our legacy. We want to honor our treasured parents, Art and Ruth Rosinsky, and our precious ‘bubbe’ [grandmother] Sara Silver, along with our beloved late husbands George Wallace and Bob Freedman. What better way to do this than to include City of Hope in our estate plans, hoping that our loved ones will be remembered and our gift will fund new discoveries and help City of Hope find a cure for cancer?”

Breakthrough Drug
Shows Results in
Lung, Colon Cancer

BY MICHAEL EASTERLING

A new drug being investigated by Marwan Fakih, M.D., professor in the Department of Medical Oncology & Therapeutics Research and medical director of the Judy & Bernard Briskin Center for Clinical Research, is “potentially practice-changing,” Fakih said.

Fakih’s phase 1 trial targets the KRAS G12C mutation with AMG510, a drug that suppresses tumor growth when taken orally. KRAS G12C is a cancer-associated gene mutation that occurs in around 13% of nonsmall cell lung cancer cases, as well as 3 to 5% of colorectal cancers and up to 2% of other solid tumor cancers, including pancreatic. It was long considered impervious to medication due to its spherical shape.

Twenty-nine patients were enrolled in the trial, including 10 patients with lung cancer, 18 patients with colorectal cancer and one patient with appendix cancer. Nine of the 10 lung cancer patients showed a clinical benefit, with five patients having partial responses and four patients having stable (nonprogressive) disease. Five had tumors shrink in size by at least 50%. Among the 19 patients with colorectal and appendiceal cancer, 14 patients experienced stable disease.

No serious side effects were reported, and treatment-related adverse events were uncommon.



Marwan Fakih, M.D.

CITY NEWS PICTURE *the* PAST



DISRUPTIVE MEDICINE

Once it was discovered that radiation could be used to fight cancer, City of Hope's **Melville Jacobs, M.D.**, collaborated with Caltech researchers and nuclear scientists to develop the Cobalt 60 Teletherapy Unit in 1955, which could deliver powerful bursts of radiation to malignancies deep within the human body.

ourHOPE

ourHope is City of Hope's personal fundraising website and a way for you to directly support the cause closest to your heart.






OURHOPE MAKES IT EASY TO RAISE MONEY FOR CITY OF HOPE

I work with some of the most amazing people here at City of Hope. **Dr. Behnam Badie** and his team inspire me every day through their passion, compassion and dedication to their patients. To support their research, I created an **ourHope** page and sent it to everyone I know, not only to raise more money but to spread awareness about brain cancer. **ourHope** enables me to be a part of this mission even though I'm not a doctor or scientist, helping to fund research and treatment and to further education.

— Paola Mork

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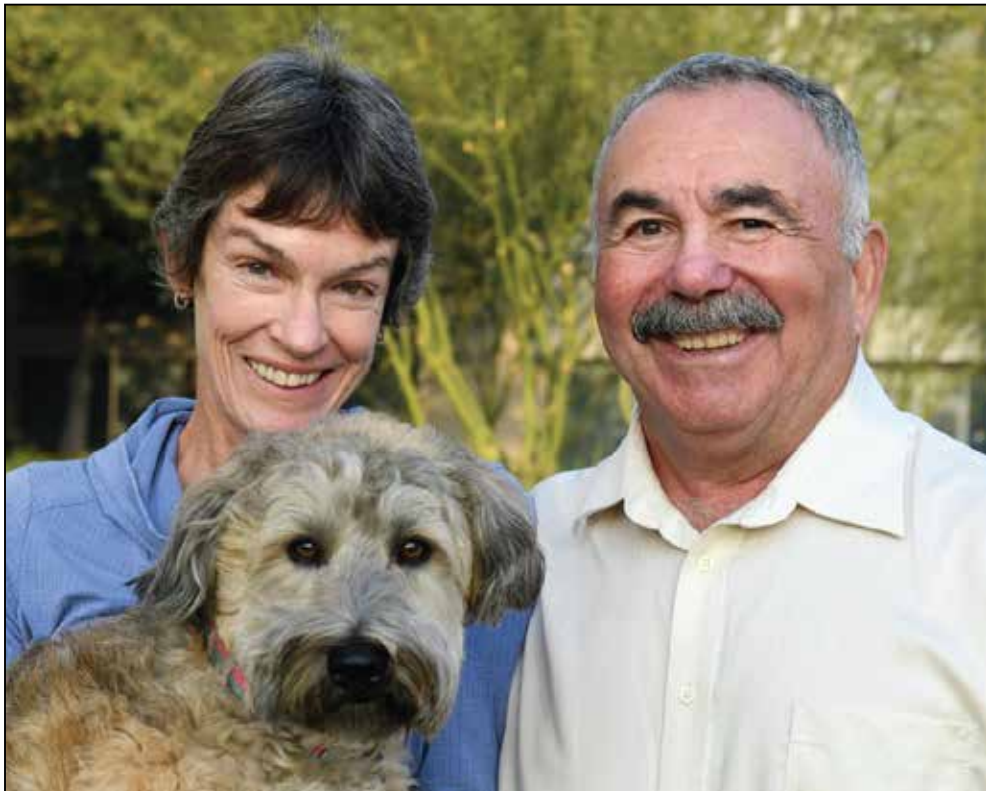
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"City of Hope is a place that saves lives. I know, because I'm one of the people whose life they've saved."

— Chuck O'Shea

Legacy of Hope Society members Eileen and Chuck O'Shea and their dog, Maggie. They have created a lasting legacy of hope and healing with a gift to City of Hope in their will.

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FOR CURING
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