# Cityof Hope.

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FROM INSULIN TO IMMUNOTHERAPY, THIS IS The Science of Saving Lives

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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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Vice President, Communications and External Affairs

AIMEE CHRISTIAN, Ph.D.

Associate Vice President, **Executive Creative Director ROB SILVERMAN, M.A.** 

Director, Content JOSH JENISCH

Director, Design DICRAN KASSOUNY, M.F.A.

Sr. Manager, Content SAMANTHA BONAR

Copy Editor LAURIE BELLMAN

Printing LITHOGRAPHIX INC.

Writers DORY BENFORD SAMANTHA BONAR MICHAEL EASTERLING MAXINE NUNES ABE ROSENBERG **ROBERT YOUNG** 

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

t City of Hope, we fervently believe that in conquering cancer and diabetes, we can change the course of the world, one special, unique life at a time. Our research and discoveries have restored millions of lives devastated by these diseases, and we are working hard to close

in on cures.

In these pages, you will read about our pursuit of new lines of research, which has led to major innovations like synthetic insulin and new approaches to CAR T cell therapy. You will learn how our whole-person approach to care means our patients are better prepared for life after cancer – body, mind and soul. You will see how we are purpose-built to turn innovative science into practical benefit as quickly as possible.

Our urgency is driven by the families, friends and loved ones – millions of people across the globe – who are diagnosed with cancer and diabetes each year. For many of us, the cause is personal. We know that there is no time to waste.

We are honored to count on the commitment and philanthropy of thousands of benefactors, advocates and supporters to advance the science. Every time a life is saved, every time a family is made whole, every time hope pushes out despair, it is because of your generosity.

Thank you on behalf of all of the patients and families whose lives you save.

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

# CUBBUZZ Spiritof Life®

The 2018 Music, Film and Entertainment Industry group's Spirit of Life® dinner was a real showstopper. Jon Platt, chairman and CEO of Warner/Chappell Music, was presented with The Spirit of Life Award and rallied more than \$6.2 million of support during this year's campaign. The festivities were hosted by 11time Grammy Award-winning artist, songwriter and producer, and close friend of Platt, Pharrell Williams. Power couple Jay-Z and Beyoncé was also on hand to honor Platt, and Beyoncé performed a stunning four-song set.



Counterclockwise from top: Beyoncé performed a four-song set; recording artist Jay-Z; Spirit of Life honoree Jon Platt (left) with recording artist Pharrell Williams; singer-songwriters Rita Ora (left) and Usher.

Photos by Kevin Mazur, Emma McIntyre

# **Rose Parade**

For the 2019 Rose Parade theme, "The Melody of Life," City of Hope named its 47th float "Harmony of Hope." City of Hope fosters harmonious collaboration between different departments, academic disciplines, research efforts and physicians to speed scientific advances from the laboratory bench to the patient's bedside. Music plays an instrumental role in patients' lives and recovery. It helps them heal, brings them comfort and gives them a temporary reprieve from treatment side effects.





# Walk for Hope

On Nov. 4, cancer survivors and supporters gathered to take part in City of Hope's annual Walk for Hope. Bob Chapek, chair of Disney Parks, Experiences and Consumer Products, served as event chair and led the more than \$1 million campaign to benefit the fight against women's cancers. The 2K/5K walk took place on City of Hope's main campus in Duarte, California.



Joanne Mortimer, M.D., and Bob Chapek

# 15,000 Second Chances

# BONE MARROW TRANSPLANT PROGRAM CELEBRATES FOUR DECADES OF INNOVATION

# BY MICHAEL EASTERLING AND SAMANTHA BONAR

City of Hope's bone marrow transplant program recently performed the procedure on its 15,000th patient, a remarkable milestone considering that the initiative started with just two physicians, three beds and guarded expectations in 1976.

Forty-three years ago, a young college student from Indiana was admitted as a patient and became the hospital's first successful bone marrow transplant.

In October of that year, the student, then 27, received the devastating news from his physician that he had acute myeloid leukemia (AML). In those days, an AML diagnosis was grim — most would say hopeless. Bone marrow transplantation (BMT) as a cancer treatment was still primitive and not in wide practice. At the time, City of Hope was one of only six medical centers in the United States offering it.

The student's doctor advised the young man to get his affairs in order, and he broke the devastating news to his family. It was a cousin, a doctor living in Los Angeles, who told him she knew of a cancer treatment center in nearby Duarte that had just launched a program for BMT.

# A HISTORIC FIRST

Trusting his cousin's advice, the young man came to City of Hope for a BMT. His eldest brother was selected as a match. He underwent a BMT as a patient of Karl Blume, M.D., who established the BMT program at City of Hope in 1975 with Ernest Beutler, M.D. Standard treatment in 1976 meant he would endure very high doses of chemotherapy followed by three-hour nonstop sessions of full-body radiation (today, targeted radiation is administered in short sessions over a matter of several days). Following the transplant, he then spent a month in isolation.

His cancer in remission, he returned to school to complete a degree in computer science. The student was one of City of Hope's longestsurviving BMT patients, for 35 years. He would remain in remission for the rest of his life, passing away in 2011.

Since then, City of Hope's laboratory and clinical researchers have led the way in making transplants more effective and safer, with fewer side effects. Having performed 15,000 transplants, from just six in 1976 to over 800 last year, the program is now one of the largest and most successful in the United States. Today, City of Hope has the most prodigious BMT program in California, with 720 annual transplants, on average. It is one the three largest programs in the country.

As for other patients who have made an impression among the thousands treated over the last four decades, "They all are memorable for me," said Stephen Forman, M.D., the Francis & Kathleen McNamara Distinguished Chair in Hematology and Hematopoietic Cell Transplantation, who came to City of Hope in 1978 specifically to work with Blume and help develop the new BMT program. "I believe that there's an inspiring story in every person's life. You just have to pause, listen, watch, help — and you will be privileged to be part of it."



# Determined to Make a Difference

Developing a world-renowned bone marrow transplant program requires vast amounts of curiosity and drive, traits shared by a longtime supporter of City of Hope's work in blood cancer, Norbert



Norbert Gehr

Gehr and the Gehr Family Foundation.

A determined, inquisitive entrepreneur, Gehr was willing to work seven days a week — and cross continents — to pursue his dreams.

"I thrive on challenges, that's what makes me tick," he once said.

So, when faced with a diagnosis of leukemia in 2014, he traveled to City of Hope for a bone marrow transplant. At the same time, he laid the groundwork for future breakthroughs in leukemia research with the establishment of the Gehr Family Foundation. Among other causes, the foundation invests in innovative medical science — including its gifts to launch the Gehr Family Center for Leukemia Research at City of Hope in 2015. Gehr lost his battle with leukemia in February 2015.

"Norbert knew more discoveries were coming, but his illness was too advanced to benefit. His wish was to help in finding a cure for leukemia," said David Lifschitz, a trustee of the Gehr Family Foundation, president and CEO of the Gehr Group and Gehr's colleague for 22 years. Keeping his eye on tomorrow while taking risks today was one of Gehr's best-known traits.

Breakthroughs underway in various stages of clinical trials at the center include immune cells engineered to stick to leukemia cells and kill them, a vaccine that may help patients avoid deadly infection, personalized treatment using math-based predictions, looking into ways to fortify the immune system to fight traces of the disease, the development of more targeted radiation with fewer side effects, innovations in bone marrow transplants, exploring how dietary changes may affect survivorship, and new drug combinations that block the growth of cancer cells. Researchers, led by Guido Marcucci, M.D., director of the center, are also tackling treatment-resistant acute myeloid leukemia with a promising new drug.

"Love what you do," Gehr said, "and excellence will follow." It's a philosophy the Gehr Family Foundation now continues in his name.

# **REFINING THE TECHNIQUE**

The advent of BMT marked an important step forward in the battle against leukemia, lymphoma and other diseases of the blood and immune system, and City of Hope has played a crucial role in the advancement of the procedure. The therapy establishes a new, disease-free blood and immune system by transplanting healthy blood stem cells into the body after destroying the patient's unhealthy bone marrow. In the first procedures, stem cells were collected exclusively from a matched donor's bone marrow. As medicine advanced, two difference sources for stem cells were discovered: peripheral blood (from the bloodstream) and umbilical cord blood. An autologous transplant uses stem cells from the patient's own blood.

When the program started, because of the physically challenging nature of the procedure, transplants were rarely performed in patients over the age of 30. Now, with refinement of the technique, "We no longer have age as a barrier," Forman said.

City of Hope was one of the first institutions to do BMTs in people over the age of 50. It was able to do this by developing an approach based on the idea of a reduced intensity, or "mini" transplant This breakthrough

method relies less

or "mini" transplant. Rodrigo Nuñez, left, with City of Hope's George Somlo, M.D. Nuñez, now a City of Hope This breakthrough nurse, received his BMT at City of Hope 42 years ago.

on heavy doses of chemotherapy and radiation and more on the antitumor effects of the graft itself (called the graft-versus-tumor effect).

"Given that many of the diseases that we take care of are diseases of older people, being able to transplant patients successfully in their 70s is a huge innovation," Forman said. Patients as young as 4 months and older than 80 years old have received BMTs at City of Hope.

In addition, "City of Hope was one of the first places to show that you could do BMT safely in patients with HIV," Forman said, performing its first transplant for AIDS-related lymphoma in 1998. Today, BMT is sometimes used to treat selected solid tumors as well as numerous nonmalignant diseases, including genetic disorder such as sickle cell disease and autoimmune diseases such as lupus, scleroderma and multiple sclerosis.

With the advent of nonrelated matched donors and, most recently, partially matched donors, BMT is saving more lives than ever before. "One of the biggest innovations derived from research is the ability now to do transplants from half-matched family donors," Forman said. This development has greatly expanded the pool of people who the Foundation for the Accreditation of Cellular Therapy, considered the standard of excellence for blood and BMT programs in the United States.

are eligible to receive BMTs, particularly among minority patients, who traditionally have had more

**BECOMING ONE OF THE BEST** 

City of Hope's BMT program is the only one in the

nation that has had one-year survival above the

expected rate for 14 consecutive years, based on

analysis by the Center for International Blood and

This is a risk-adjusted survival benchmark, so the

fact that City of Hope traditionally manages the

most difficult cases and still has outcomes that

The institution has also earned accreditation by

exceed expectations is especially remarkable.

difficulty finding matches.

Marrow Transplant Research.

# A HUMANISTIC APPROACH

Looking forward, the program is focused on minimizing the side effects of the procedure, increasing its effectiveness and expanding its reach. These include clinical trials of a City of Hopedeveloped vaccine for cytomegalovirus (CMV), a common and potentially deadly infection following transplant, and incorporating CAR T therapy, an immune-boosting treatment used either before transplant to put the disease into remission or after transplant to help prevent recurrence. (Even before the current vaccine trials, City of Hope's program was one of the first to develop a treatment for prevention of CMV infection after transplant, which has nearly eliminated the threat of CMV for BMT patients.)

"What's really differentiated our program is all this is wedded to a deeply humanistic vision of delivering care to the patient," said Joseph Alvarnas, M.D., associate clinical professor in the Department of Hematology & Hematopoietic Cell Transplantation at City of Hope. "We have a system in which not only do you have hematologists caring for their patients, but you also have them partnering very carefully with members of supportive care medicine, from palliative care physicians to social workers to psychologists — and all of those things create a much more grounded, human-centered vision."

The "Celebration of Life" BMT reunion is an annual highlight at City of Hope, bringing together more than 7,000 attendees each year, a tradition that began 43 years ago. In addition, City of Hope established a formal long-term, follow-up program in 1998 to maintain communication between patients, families and physicians and to track outcomes so that the hospital is aware of the kinds of problems, both physical and psychological, that some patients have following transplant.

"It can be somewhat overwhelming if you think about it: 15,000 transplants!" Forman said about the program's profound evolution over the last four decades. "I only stop and think about it when someone asks me about it. I forget how long it's been and how much we've accomplished. My focus is, What does this patient need today? There's a thrill when you see the possibilities of what you can do for someone that you couldn't do before. It's very inspiring."

"Once we extend our hand and grasp yours, we do not let it go," he said.



Acute myeloid leukemia patient Ian MacLeod (left) with his brother — and donor — Adam

# Care for the *Body, Mind, Soul and Spirit*

arcia and Jim Brammer are active members of the City of Hope Board of Governors, a group of volunteers who raise funds for research at City of Hope to fight life-threatening diseases. But their relationship with City of Hope began when their son Brian Lambert was treated here for acute myeloid leukemia, ultimately receiving two bone marrow transplants. By the time they met Stephen J. Forman, M.D., the Francis & Kathleen McNamara Distinguished Chair in Hematology and Hematopoietic Cell Transplantation, Brian had already undergone a round of treatment elsewhere. Coming to City of Hope was a transformational experience for the whole family.

"The difference we experienced is because City of Hope is driven by caring for not only the body but the mind, the soul and the spirit. We were amazed by the treatment our family received," Marcia said. "Not only from Dr. Forman — who is a remarkable man with a heart that goes along with the brilliance of his mind — but from everyone we encountered.... They treated us as if Brian was their own child."

Brian is now a member of City of Hope's Music, Film and Entertainment Industry group. In June 2018, Brian and his family had the remarkable experience of meeting the young man whose donation saved his life. Jim recalls the moment he was able to ask this man why he became a bone marrow donor for someone he had never met: "He smiled as he told me that it was just the right thing to do." The family still keeps in touch with this generous young man.

The Brammers have been tireless in advocating for City of Hope. They are particularly involved in introducing City of Hope's work to younger philanthropists through a City of Hope fundraising chapter called 25 to 5, which they co-founded with fellow Board of Governors' member Lisa Sherman. Their goal is to start building the next generation of leadership and support for City of Hope by connecting younger supporters with City of Hope's leading-edge research.

Jim and Marcia are happy to know that they will be able to continue their support far into the future, as they have named City of Hope a beneficiary of their trust. "We want to make sure that City of Hope has what it needs to go forward to do all its incredible work."

Learn about easy ways to create your legacy of hope at **myplanwithcoh.org.** 



Jim and Marcia Brammer



### **BY ABE ROSENBERG**



athan Dotson was worried.

A routine physical exam in 2014 revealed a high PSA level, suggesting possible prostate cancer. A few scans and biopsies later Dotson, got the bad news.

His cancer was advanced, it had spread to his bones and the outlook was grim.

No traditional cancer-fighting treatment would do him much good. There is no cure for advanced metastatic prostate cancer. Some drugs may temporarily slow the cancer's growth and spread, but prostate cancer cells eventually adapt, rendering even those treatments ineffective.

"I was down and depressed," Dotson remembered. He contacted several institutions, looking for a second opinion, hoping for a better outcome. "Everyone said they couldn't help me."

Then he called City of Hope.

## **CRITICAL TRIALS**

A nurse who spoke with Dotson on the phone guided him to a clinical trial of a new hormone therapy designed to help rid the body of testosterone, which fuels prostate tumors.

"I didn't know anything about clinical trials," said Dotson. But he liked what he heard, and soon he

began taking the still-experimental drug, paired with regular injections of the standard treatment.

In taking that step, Dotson joined a vital community of City of Hope patients who not only receive leading-edge, potentially lifesaving, not-yet-generally-available therapies, but also earn praise and gratitude for doing so.

"My clinical trial patients are my heroes!" said Tanya Dorff, M.D., an internationally recognized leader in prostate cancer. Working closely with City of Hope research scientists, Dorff maintains an extensive clinical trials portfolio with a special emphasis on immunotherapy and the formidable potential of chimeric antigen receptor (CAR) T cell therapy. In the process, she treats many patients just like Dotson, and she knows how much she owes them.

"I'm so grateful for the value they add to my work," she said. "And I honor the faith they have in me, the trust they've put in me. I can't do any of this without them." City of Hope teams put approximately 1,000 new patients on therapeutic trials each year, and without those bonds of faith, trust and gratitude, none of it could happen.

That's because patients who sign up for clinical trials are helping doctors and

researchers gain critical knowledge not obtainable any other way.

Not surprisingly, people have misconceptions, and if you've ever thought about a clinical trial for yourself or a loved one, no doubt some of these fears have crossed your mind: The fear that you'll be simply a "guinea pig," that your doctor will care more about advancing the new drug than about you, that you'll be given something dangerous or a placebo instead of a real treatment, or that clinical trials are only for "last resort" patients with nothing left to lose.

Wrong all around, say the experts.

# A FOCUS ON THE INDIVIDUAL

"Our most important focus is the individual, not just the disease," said Steven T. Rosen, M.D., City of Hope's provost and chief scientific officer and the Irell & Morella Cancer Center Director's Distinguished Chair. "While historically trials were experimental 'last option' procedures, we've evolved dramatically. Now they are an opportunity to provide the best therapies, to help our patients beat cancer and improve their quality of life."

"Some of our most innovative trials right now target the early stages of disease," added Dorff, who never looks at a patient as a guinea pig. "I'm super enthusiastic about every trial I run. I never ask a patient to do anything I don't think will help, and I never give them anything I wouldn't take myself or give to someone in my family."

By the time a proposed treatment has reached the human trial phase, it has gone through years of rigorous research and testing, along with a slew of federally mandated procedures and protocols designed to protect patients every step of the way. For every potential drug that makes it to a clinical trial, about 1,000 do not. "Each of our trials has been vetted by a huge number of people," said Dorff.

Placebos are being used less frequently in cancer trials, most commonly in scenarios where standard treatment alone is being measured against standard treatment and a new drug. Placebos are not used in place of effective cancer therapy. They are used to see whether a new drug improves success when added to standard treatment, or in situations where no effective treatment exists.

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"Our most important focus is the individual, not just the disease."

Steven T. Rosen, M.D., City of Hope's provost and chief scientific officer



Patient Norman Pawchuck is greeted by his clinical trial nurse, Kaelyn Armenta, R.N., at the new Judy & Bernard Briskin Center for Clinical Research.

## A SENSE OF URGENCY

City of Hope's program is special because it was built with the same core values as the institution itself: an urgency to find the best treatments; a multidisciplinary approach; and an emphasis on leading-edge medicine, compassionate care, rapid bench-to-bedside research and always putting the patient first.

Even lab workers who never see a patient get the message.

"I always tell the research operations team, 'Never assume your work isn't patient-focused. Every time a clinician is with a patient, you're in the room with them!" insisted Ashley Baker Lee, senior vice president of research operations. "Every one of our doctors is backed by hundreds of professionals who make it possible."

Since joining City of Hope in 2012, Baker Lee has made it her mission to optimize the trials process in order to get more lifesaving drugs to more patients faster and more efficiently. Her job is maddeningly complex, painstaking and unending — reorganizing departments, building staff, dismantling data silos — but she's seeing results. Five years ago, a typical trial activation timeline — how long it takes to process the many components

involved with getting a trial started — could run seven months or longer. City of Hope has reduced the time to fewer than 90 days.

"What we're giving our patients is time," she added, emphasizing that cancer patients can't wait, and everything must be done to help them as rapidly as possible. The mission is personal to Baker Lee: She's watched both parents struggle and pass away from cancer, and she herself has been on a clinical trial.

"If I can help move us forward to a cure, I'll have made my mark."

### LABOR OF LOVE

For Dotson, the trials program was a perfect fit at the perfect time. The drugs he received lowered his PSA to zero and, nearly five years later, that's where it remains. He's still on the experimental treatment, he feels great and he's optimistic about his future.

"I'm one of the lucky guys," he said. "I know this drug may not always work, but the doctors have told me about even newer treatments in the pipeline.

"When I was at my lowest, City of Hope gave me hope. They're really good at that. And now I feel like I could live forever!"





# A Star Is Born

*Inside the Judy & Bernard Briskin Center for Clinical Research lies the future of medicine.* 

## BY MICHAEL EASTERLING

t's a place where groundbreaking discoveries will be made and treatments developed that we can speed to patients who cannot wait. One such patient is Los Angeles Fire Department Captain Matthew Gatewood.

A patient of Amrita Krishnan, M.D., director of the Judy and Bernard Briskin Center for Multiple Myeloma Research, Gatewood was diagnosed with multiple myeloma in October 2006 at another institution and was told that he had two to five years left to live. He decided to come to City of Hope for a second opinion.

# 'THIS IS WHERE I BELONG'

"When I met with Dr. Krishnan, I told her what my other doctors had said," Gatewood recounted. "She said to me, 'Mr. Gatewood, I have reviewed your charts and nowhere do I see a date of death indicated.' I knew at that very moment that this is the place where I belong."

Gatewood is still on active duty as a firefighter. He had a stem cell transplant in 2011 when his cancer started to progress, and received a second transplant in 2014. He then participated in a clinical trial funded by the Briskin family. He has been

on another Briskin-supported trial medication for the past year and reports that "things are looking good."

Judy and Bernard (Bernie) Briskin attended the ribbon-cutting ceremony for the new center and had the opportunity to meet Gatewood.

"It is so incredibly heartwarming to hear directly how this wonderful new building is having such a positive effect on so many lives, including yours, Captain Gatewood," Judy Briskin said. "We are so honored to partner with City of Hope to open this new facility. Our partnership is deeply rooted in our confidence that City of Hope has innovative ideas, transformative therapies, lifesaving treatments and overall medical excellence. The new Briskin Center for Clinical Research has the power to transform lives and create hope for the many people who will walk through its doors. We are profoundly proud to have our name immortalized in this special place where medicine, science and compassion come together to save lives."

# A CENTER FOR HEALING

The Briskin Center includes 17 private and semiprivate infusion areas, many of which overlook the Rose Garden and sculptures of Pioneer Park — as well as two nursing stations, and three exam and procedure rooms. The state-of-the-art center has numerous patient-centered features, including

"With this new center, you're saving thousands of lives at a time."

Matthew Gatewood, Los Angeles Fire Department captain iPads that enable patients to regulate lighting, listen to music and watch online content that is streamed to a flat-screen monitor. It also includes onsite pharmacy and lab services, a dedicated registration site, and outdoor seating for patients and their families.

In addition, more of the treatment tasks, such as EKG, respiratory therapy and lab testing, are now completed at this same location, with clinicians and staff who are knowledgeable about each specific treatment. This provides all staff working with the Briskin Center with a better understanding of the trial protocols, and enables teams to work more collaboratively to handle other complex study tasks with greater ease. There is also a compounding

pharmacy onsite, so that clinical trial therapies and related treatments are only a few steps away from the patients who need them.

The new location provides the medical team — led by Briskin Center Medical Director Marwan Fakih, M.D., and Co-medical Director Leslie Popplewell, M.D. with the very best opportunity to explore how new drugs and therapies will interact with the body and fight disease.

This is a fight that Gatewood is counting on, as he continues his treatment at the new center.

"I stand here today because of the heart, compassion, the love and humanity of family," he said. "My City of Hope family and the Briskin family. As firefighters, we typically save one person at a time. But with this new center, you're saving thousands of lives at a time. And for that, I say thank you." Thirteen out of 13 patients evaluable for response received the treatment and are in complete remission, showing a 100 percent response rate with no significant increase in toxicity.



### **BY DORY BENFORD**

Click here to learn more about how CAR T cell therapy uses your own immune cells to fight cancer.

achieves complete remission in patients with acute lymphoblastic leukemia about 80 percent of the time; however, a large proportion of these patients have side effects such as cytokine release syndrome and neurotoxicity. Samer Khaled, M.D., associate clinical professor in the Department of Hematology & Hematopoietic Cell Transplantation at City of Hope, said he may have found a CAR T product that is more potent and less toxic — a potential game-changer if the early results of his ongoing phase 1 clinical trial hold through future testing.

CAR T cell therapy reportedly

### YOUR OWN WORST ENEMY

CAR T cell therapy, a kind of immunotherapy, involves removing a patient's T cells from his or her blood and adding a chimeric antigen receptor that is designed to seek out cancer cells. These engineered T cells are then infused back into the patient's body using an IV, where they can attack and kill cancer cells.

So far, the clinical trial has enrolled 16 patients with relapsed or refractory B cell acute lymphoblastic leukemia, a disease that has poor survival rates. Investigators used a unique manufacturing platform developed at City of Hope that generates therapeutic cells from enriched memory and "naïve T cells" immune soldiers known for their capacity for long-term persistence.

Thirteen out of 13 patients evaluable for response received the treatment and are in complete remission, showing a 100 percent response rate with no significant increase in toxicity. One of those patients is Tyler Routh.

### A SCARY DIAGNOSIS

In January 2014, Routh was diagnosed with acute lymphoblastic leukemia.

"I had some back pain that got progressively worse with weakening legs and numbness. My chiropractor was getting me set up for an MRI, but it wasn't going quickly enough. Eventually, I could not get around without a cane, then within a week, I was using a walker and then couldn't get out of bed," Routh recalled.

"An ambulance had to take me to the emergency room, where I had an MRI done. After that, I went into surgery to have a tumor removed from my spine. There was no guarantee that I would walk again at this point, and I hadn't even been diagnosed with cancer yet. The tumor samples were sent to the lab for a few days and that was where they found my diagnosis."

After his surgery, Routh underwent more tests, radiation and chemotherapy. He also underwent physical therapy and had to learn how to walk again. Despite these challenges, he was pronounced cancer-free and went on with his life, only for the cancer to come back in 2016.

## **AN EXPERIMENT IN HOPE**

"I had been cancer-free for almost two years. I was walking around healthy. Then, I started experiencing some weird muscle spasms in my legs," Routh said. "After some testing, we discovered that I had relapsed and this time it was in the marrow."

Routh went through chemo again, but this time, it didn't work as well as he had hoped. That's



Tyler Routh, left, with his doctor, Samer Khaled, M.D. A clinical trial using CAR T cell therapy put Routh's ALL into remission.

when his care team began considering clinical trials. Like many patients, Routh was nervous about turning to clinical trials.

The idea that clinical trials are experimental treatments is prevalent, but it takes a great deal of work to get a treatment to the trial phase. For a drug to enter clinical trial, there has already been a tremendous amount of work. Every single Food and Drug Administration approved drug used in the clinic was once in clinical trial at some point. And there are often benefits to joining clinical trials, which Routh was about to discover.

# WAITING FOR GOOD NEWS

"There were talks of clinical trials, and those words scared me more than cancer and chemo did originally, but it led me to City of Hope. CAR T cell therapy was the new trial that seemed promising for my situation, and I fit the criteria perfectly," Routh recalled.

"I was nervous at first to get used to a new, bigger hospital, but now it feels welcoming, like a second home. It's such a nice campus, with an amazing staff. The rooms in Helford Hospital are wonderful, and there is plenty of space to roam. I also liked that the meal service was all at my convenience rather than set times. I visit the koi pond every time I have an appointment."

In addition to feeling at ease at City of Hope, the efficacy of his CAR T treatments was also a pleasant surprise.

"I had my infusion on November 28, 2016, and at my 30-day scan and bone marrow biopsy, I was cancer-free. I still am to this day," Routh said.

Now, Routh is waiting for just one more piece of good news from his doctor.



**Tyler Routh** 

"I still haven't had sashimi, poke or oysters in over two years and I'm really hoping to get approval to eat that again from the doctor soon," Routh said.

Sushi aside, Routh's cancer battles have also resulted in some permanent nerve damage to his feet. He also struggles with the feeling that his life was placed on pause for a couple years. Overall, however, this experience has given him a positive outlook on life.

"This process has taught me a lot about health care.

medicine and science. It's also made me focus on my health a lot more and reminded me to do the things you want to do before it's too late."

Thanks to CAR T cell therapy, Routh now has plenty more time to live his life to the fullest.

# Kine and the second sec

publishing of research by Arthur Riggs, Ph.D., and Keiichi Itakura, Ph.D., that led to the development of the world's first synthetic insulin.

# BY MICHAEL EASTERLING

In January 1979, the National Academy of Science published a paper about an innovative discovery at City of Hope that forever changed how diabetes is treated. Arthur Riggs, Ph.D., and Keiichi Itakura, Ph.D., revolutionized diabetes treatment when they used a synthetic DNA chemistry and recombinant DNA technology to make a novel gene, one that coded for human insulin. It would be the first human gene deliberately designed to make a useful product.

"Up to that point, human insulin was not available. Insulin mainly came from cows," explained Riggs of the team's "eureka" moment. "We didn't copy the natural gene. We made our own."

Building on work from MIT scientist Gobind Khorana, Itakura developed a technique that reduced the time needed for successful synthesis from years to weeks. Riggs and Itakura, together with their colleague Herbert Boyer at University of California San Francisco, demonstrated that when introduced into bacteria, their human-designed gene functioned well, causing the bacteria to make human insulin.

"Not only did we make that gene, we designed it to command bacteria to make insulin," Riggs said.

The groundbreaking discovery — and invention — by Riggs, Itakura and their colleagues provided a new source of insulin that would become the first biotechnology ever approved by the U.S. Food and Drug Administration (FDA). Their landmark research was published in the January 1979 issue of *Proceedings of the National Academy of Science* (PNAS). The work was funded by then-startup biotech company Genentech, which improved yields and then transferred the technology to Eli Lilly to scale up production. By 1982, the synthetic insulin was available commercially, branded as Humulin. It is now the standard of care for

> Facing page: Arthur Riggs, Ph.D., and Keiichi Itakura, Ph.D. Inset: Itakura and Riggs, 1979



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# Cityof Hope

diabetes, helping millions of people worldwide each year.

Both Riggs and Itakura continue their legendary careers at City of Hope. Itakura has been here since 1975, becoming a professor 1980 and forming the Department of Molecular Genetics (which we now call the Department of Molecular and Cellular Biology) in 1982. He is currently a professor in the department. His work in recombinant DNA technology has significantly impacted the fields of molecular biology and biochemistry on a global scale.

Specializing in epigenetics and gene regulation, Riggs's cancer research has also been groundbreaking, with novel treatments produced for breast, colon and blood cancers. He currently holds the Samuel Rahbar Chair in Diabetes



TO SAFE BIOLOGICAL FACTORY



& Drug Discovery, and is director of the Diabetes & Metabolism Research Institute at City of Hope. He is founding dean of the Irell and Manella Graduate School of Biological Sciences, and director emeritus of Beckman Research Institute of City of Hope. In addition to the 40th anniversary of the published research, Riggs also marks his 50th year here at City of Hope, joining us in 1969.

Last year, Riggs received the Chancellor's Award Medallion from his alma mater, University of California Riverside, for his "extraordinary achievements." He calls his 50 years here "the best job in the world."

Congratulations to Riggs and Itakura on the 40th anniversary of the publication of a landmark achievement in medicine and research

# **INSULIN:** THENAND MOU **BY ABE ROSENBERG**

efore 1922, a diagnosis of type 1 diabetes was a death sentence.

Patients with this mysterious metabolic disorder couldn't process nutrients from food. Dangerous levels of glucose accumulated in their systems, damaging vital organs. These unfortunate people faced a short, bleak future, punctuated by blindness, loss of limbs, strokes, heart attacks and kidney failure.

Adults might live two years. Children, even less.

# **A BREAKTHROUGH CHANGES EVERYTHING**

The development of insulin and the methods to derive it safely from cattle and pigs saved many lives but also created new challenges. With diabetes no longer a fatal disease, the number of living diabetics rapidly grew and expanded into subsequent generations, because type 1 diabetes can be passed down to children.

Animal-derived insulin was a less-than-perfect solution. Because it's not an exact match to human insulin, some patients had allergic reactions to it. And it was costly, requiring 8,000 pounds of animal pancreases to make one pound of insulin. Aside from the ethics of killing so many animals, it was feared that the rapidly increasing population of diabetics would eventually create an insulin shortage.

Arthur Riggs, Ph.D., and his groundbreaking research changed everything.

In 1978, using the still-new technology of genetic engineering, Riggs and his colleagues at City of Hope and Genentech chemically combined DNA fragments of human insulin and attached them to E. coli bacteria, which "switched on" the genes, a process that formed a complete insulin molecule identical to that produced by the human body.



Arthur Riggs, Ph.D., circa 1979

# A 'HUGE IMPACT'

Riggs, the Samuel Rahbar Chair in Diabetes & Drug Discovery, knew he was onto something big.

"I was hoping that what we were doing would work," he recalled. "If it did, then, yes, I knew it probably would have a huge impact."

### Huge, indeed.

Creating synthetic human insulin meant there would now be a potentially unlimited supply of this lifesaving drug with none of the drawbacks of its animal-based predecessors. The process also made further refinements and improvements possible and they came quickly, from pens and pumps to super-engineered "analogues" that improve the way insulin is metabolized.

Still, some 40 years later, success is not complete. Forty-thousand new cases of type 1 diabetes are diagnosed every year in the U.S.

Which is why Riggs keeps on working.

"Insulin or insulin analogues is not a cure of diabetes," he said. "What is needed is something to prevent, reverse or stop the progression of diabetes. This is what I am still working toward and hope to see accomplished in my lifetime."

# Turning Pancreatic Cells into Insulin Producers

Recent papers co-authored by Wanek Family Project director show new promise for a range of treatments

ne of the major challenges in developing treatments for type 1 diabetes (T1D) is understanding the mechanisms behind how the immune system mistakenly destroys beta cells — the cells that make

destroys beta cells — the cells tha insulin — to cause T1D.

A paper published in the Feb. 13, 2019, edition of the journal *Nature* explores new ways of replacing beta cells after too many of them have been killed by the immune system, and in a way that makes them less attractive to the immune system's urge to eradicate them.

The paper, "Diabetes relief in mice by glucose sensing insulin-secreting human  $\alpha$ -cells," outlines work done by an international team of researchers, including Bart Roep, Ph.D., the Chan Soon-Shiong Shapiro Distinguished Chair in Diabetes and the founding chair of the Department of Diabetes Immunology within the Diabetes & Metabolism Research Institute at City of Hope. Roep is also director of the Wanek Family Project for Type 1 Diabetes at City of Hope, an initiative aimed at creating powerful new approaches to curing T1D.

"Different sources of new beta cells exist, and many of these are also present in patients with T1D," Roep explained. "We found that human pancreatic alpha cells can be engineered to be turned into insulin producers, which in turn reversed diabetes, curing the disease in mice."

Furthermore, these pseudo beta cells are less likely to provoke an immune response than the original beta cells, meaning they may be able to live within the same immune system that eliminated the beta cells that came before them. If true, this would help remove a considerable hurdle in islet replacement therapy. In addition, the alpha cells made to produce insulin in the study seem less stressed, another major problem that can lead to the depletion of beta cells in patients with T1D.

According to Roep, these findings could mean that doctors might be able to forge new sources of insulin without the need for organ donors one day. In fact, they may even be able to do autologous transplants, meaning they would use cells from a patient's own body that have been treated to be resistant to immune attack. Both methods would hopefully reduce the need for the immunesuppression drugs necessary for current islet transplant therapies. However, it is important to



Bart Roep, Ph.D., professor and founding chair, Department of Diabetes Immunology

note that the *Nature* study provides conceptual evidence that human islet cells could be engineered to treat diabetes; further testing is needed to see if the findings will translate in human subjects.

The *Nature* study comes on the heels of two other papers co-authored by Roep and published in *The Lancet Diabetes & Endocrinology*. The two-paper series covers the results of current and recent clinical trials for immunotherapies to deal with the immune attack on beta cells — the other end of the spectrum from the *Nature* study — and the challenges faced, as well as approaches to overcome these in the future.

The *Lancet* papers serve to shed light on the rigorous process necessary to bring new therapeutics from bench to bedside in a successful and timely manner.

These challenges highlight the urgency of finding

solutions — and the power of partnering with donors like the Wanek family. Their philanthropy through the Wanek Family Project, as well as generous investment from The Alfred E. Mann Scientific Research Foundation, Jon Platt and family, as well as others, enables pursuit of multiple avenues of research simultaneously, so we can uncover answers more quickly.

City of Hope is fortunate to partner with a longstanding and committed group of donors who intimately understand the critical nature of research, and are investing aggressively to accelerate cures.

The first paper, "The challenge of modulating  $\beta$ -cell autoimmunity in type 1 diabetes," was led by Mark Atkinson, Ph. D., from the University of Florida College of Medicine, and co-authored by Roep.

The second perspective piece, "Antigen-based immune modulation therapy for type 1 diabetes: the era of precision medicine," was led by Roep and researchers from King's College London.

Between the two papers, Roep says that some revelations were merely wake-up calls. But new facts, such as solid proof that both the disease and patients are heterogeneous, mean that no "magic bullet" therapy can be expected. Not all beta cells are destroyed, as scientists had previously believed, and T1D patients can have insulin-producing beta cells for decades after

diagnosis even if no insulin is secreted. These new findings provide new opportunities for further study.

"We also saw further evidence that T1D is not 'just' an autoimmune problem, it is a beta cell problem, where the immune system responds with good intentions to stressed tissue," Roep said. "This implies that immunotherapy alone will not be enough; we must also treat the beta cells."

He points to antigen-based therapy as a promising strategy and a positive step away from the classic immune suppression that now is standard therapy in autoimmune diseases and puts patients at risk for cancer and infection. Researchers and physicians need to negotiate with the immune system, rather than bombard it into submission, he added.

"The antigen-based therapies are very exciting and surprising to me," Roep said. "Not only is it safe, this type of therapy serves to re-educate the immune system how to do it right."

# CAR Takes On HIV

### BY SAMANTHA BONAR

he California Institute for Regenerative Medicine (CIRM) has awarded City of Hope's Xiuli Wang, Ph.D., research professor in the Department of Hematology & Hematopoietic Cell

Transplantation, \$3.8 million to develop chimeric antigen receptor (CAR) T cells that can target and kill HIV-infected cells. The treatment will also use the cytomegalovirus vaccine to stimulate the immune system to proliferate and maintain the CAR T cells.

"Our approach has the potential to change how HIV patients are treated," Wang said. "Our goal is for a person to receive this therapy once, which would make it possible for that patient to stop the anti-retroviral drug therapy regime for the rest of their lives."

Based on anti-retroviral drug therapy cost calculations, HIV CAR T therapy could provide cost savings to the health care system. Even though the cost of CAR T manufacturing is higher, the cost of the therapy per year could be significantly lower due to the singleinfusion mode of treatment.

CIRM's Grants Working Group, an independent panel of experts who review all of CIRM's applications for scientific merit, unanimously recommended Wang's initiative for the full funding requested, saying that it showed "exceptional merit, necessary significance and potential for impact."

In its review, the group said they "were very enthusiastic [about] this novel, albeit high risk, bispecific CAR-T cell therapy approach to curing or effectively controlling HIV infection. Reviewers thought that the rationale focusing on cytomegalovirus (CMV) specific T-cells and engineering them to target HIV-infected cells was based on sound scientific rationale and was supported by the preliminary data." City

Jeff Sheehy, a CIRM board member and patient advocate for HIV/AIDS, said there is a real need for a new approach to treating HIV patients. There is no cure for HIV, and only half of HIV patients adhere to anti-viral drug therapy in North America. Every year, 16,000 HIV individuals die in the U.S.

"With 37 million people worldwide living with HIV, including 1 million Americans, a single treatment that cures is desperately needed. An exciting feature of this approach is the way it is combined with the cytomegalovirus vaccine," Sheehy said. "Making CAR T therapies safer and more efficient would not only help produce a new HIV treatment but would help with CAR T cancer therapies and could facilitate CAR T therapies for other diseases."

Wang will use the CIRM funds to optimize the clinical manufacturing of the therapeutic product at City of Hope, complete the characterization of the efficacy and safety profiles of the therapeutic product, and submit the regulatory documentation to the Food and Drug Administration to initiate a clinical trial at City of Hope, hopefully within 18 months.

CIRM, California's stem cell institute, was created by the voters of California in 2004 when they passed Proposition 71, which authorized \$3 billion in funding for stem cell research in the state. The institute funds stem cell research at institutions and companies throughout California with the goal of accelerating treatments to patients with unmet medical needs.

Xiuli Wang, Ph.D. (right), in her lab with researcher Laura Lim





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City of Hope is rolling out a program called relationship-based care, or RBC, which has been described as "a philosophy, an operational blueprint and a way of being." Its centerpiece is demonstrating verbal and nonverbal forms of caring toward patients.

Developed almost two decades ago, RBC is a proven method for improving safety, quality, the patient experience and employee engagement. While RBC is being adopted institutionwide, nursing is the first discipline to implement concepts in a "wave." Wave 1 units include both inpatient and outpatient staff. They have created a vision for care, and they are currently implementing action plans to make this vision a reality on their units.

"RBC focuses on three key relationships: care of self, care of colleagues, and care of patients and families," explained Mary Perrin, B.S.N., R.N., O.C.N., B.M.T.C.N., N.E.-B.C., clinical director of the ambulatory infusion department. "All three relationships are crucial in achieving its intended results: transformational leadership at all levels, increased staff engagement and retention, care outcomes exceeding benchmarks, increased operational efficiency and exceptional patient experience."

RBC puts the focus back on the needs of the patient and family. It considers the nurse and patient/family relationship the core of a healing environment. The cornerstones of RBC are caring and communication — making sure that in all interactions, patients are treated with compassion, dignity and respect.

For nurses and clinicians, the program is designed to bring joy back into the work they do. In RBC culture, structures, processes and relationships are designed to support every team member's ability to provide attuned, compassionate, high-quality care. This means that teams are reconnected with the purpose and meaning of their work, and take ownership for providing the best possible care and service. All members of the organization are valued for their contributions and supported in continuous





learning and reaching their full potential.

"While keeping 'heart' and 'spirit' at its core, it is solid in its implementation structure," Perrin said. "All participants have clarity around concepts and purpose. Moreover, it has regularly scheduled status checks that keep staff on track with action plans. It reinforces the notion, 'Start where you are.'"

RBC uses appreciative inquiry so that an organization can identify "What is right about it?" and move on from there to reach its full potential. "Collegiality and collaboration are its cornerstones. Safety, quality and satisfaction are its products," Perrin said.

RBC comprises several fundamental assumptions, according to a January 2016 article in *Nursing Management*:

- The essence of caring is in authentic human connections.
- The heart of care delivery is the quality of relationships between patients, families and caregivers.
- A therapeutic relationship between the patient/family and a professional nurse is the core of safe, quality care.
- In order to care for others, one must have knowledge of oneself and practice self-care.
- Leaders must model and inspire ownership for care and excellence in service.
- Healthy work relationships create the conditions for caring and healing.
- Every person in the organization, no matter what role or pay scale, has a valuable contribution to make.
- Empowerment and ownership of work and practice are foundational to creating a deeply committed workforce.
- Culture transformation happens one relationship at a time.

On a practical level, some examples of RBC include centering yourself before entering a room with a patient, sitting at eye level to speak with patients, asking patients what their most important goals for care are, explaining procedures before performing them, providing reassurance, taking scheduled breaks to regroup, looking for ways to help co-workers before they ask and developing relationships with colleagues by participating in retreats.

"RBC is an exquisitely structured program," Perrin said. "We are so excited to roll it out here and see how it enhances our lives, the lives of our colleagues and the lives of those who come to City of Hope for care and healing."

# Gender and Brain Cancer:

Why do women respond better to treatment?



nationwide team of researchers that includes City of Hope's Translational Genomics Research Institute (TGen) has identified molecular differences that explain why men die of glioblastoma, a type of brain

cancer, at nearly twice the rate of women.

The study, published January 2 in the journal *Science Translational Medicine*, could help tailor drug treatments that are specifically designed for men and women based on their tumors' molecular subtypes.

"We have known for years that men contract and die from glioblastoma at a significantly higher rate than women," said Michael Berens, Ph.D., TGen deputy director, head of the TGen Brain Cancer Research Laboratory and a contributing author of the study. "We now have a much clearer understanding of this phenomenon, and this study should help us in the future to improve survival for all glioblastoma patients."

The research, led by Washington University School of Medicine in St. Louis, identified five distinct molecular signatures of glioblastoma in men, and five in women, that help explain the underlying disparities in patients' response to treatments.

"It is our expectation that this study could have

"The males did not respond as well, and we wanted to understand why, so we looked at the underlying genetics of patients" tumors," Rubin said.

an immediate impact on the care of patients with glioblastoma, as the findings indicate we should be stratifying male and female glioblastoma into risk groups and evaluating the effectiveness of treatment in a sex-specific manner," said Joshua B. Rubin, M.D., Ph.D., a Washington University professor and the study's co-senior author.

Glioblastoma is an aggressive disease, with a

median overall survival of only 15 months for newly diagnosed patients.

Studying adults with glioblastoma, researchers found that standard treatment is more effective in women than men. Researchers reviewed patient MRI scans and survival data from a cancer research database. They then calculated tumor growth velocity every two months for the duration of therapy in 63 glioblastoma patients — 40 males and 23 females — who received standard chemo-radiation treatment following surgery.

While initial tumor growth velocities were similar between women and men, only females showed a steady and significant decline in tumor growth after treatment with temozolomide, the most common chemotherapy drug used to treat glioblastoma.

"The males did not respond as well, and we wanted to understand why, so we looked at the underlying genetics of patients' tumors," Rubin said.

"Josh Rubin's results on sex differences in glioblastoma are very intriguing," said Christine Brown, Ph.D., associate director of the T Cell Therapeutics Research Laboratory and the Heritage Provider Network Professor in Immunotherapy at City of Hope. "We will be retrospectively looking at our patient response in our CAR T cell trials to see if there are any sexrelated differences."



t's hard to miss the barrage of clever advertising for home DNA tests — and the marketing works. Home DNA tests were among the top 10 holiday season gifts ordered on Amazon in 2018.

When they first came along about a decade ago, home DNA tests were offered

as a glorified form of entertainment that cranked out tidbits of information people could share at parties. But DNA analysis can tell us much more, including our risk of developing some cancers and other diseases.

23andMe, for example, provides a growing range of health-related genetic information to its customers, ranging from increased risk for breast cancer, Alzheimer's and Parkinson's disease, to whether a person is a carrier for dozens of inherited conditions like cystic fibrosis or sickle cell anemia.

It's reasonable to assume that other companies will follow this path, and with more players in the market, it will likely become easier and cheaper than ever to ship out your saliva sample in a postpaid envelope and get back a slew of reports dissecting what your DNA says about your present and future health.

# HOW VALUABLE IS THE INFORMATION?

But should you?

"This is a hotbed issue," said City of Hope's Kathleen R. Blazer, Ed.D., M.S., L.C.G.C., a boardcertified genetic counselor and educator. Blazer and her colleagues worry that customers will make incorrect assumptions about the breadth and accuracy of home tests, that they may substitute a home kit for a more complete and informative screening at a qualified medical center, and even make questionable medical decisions based on the limited information they receive.

If you've thought about trying one of those home kits, Blazer urges you to think before you spit. Even the most elaborate home test, she asserts, only scratches the surface.

"This is recreational genetics. It's very superficial, a very limited screening, not at all a thorough analysis," she said. Unlike a full screening performed by a geneticist, which reads a patient's DNA and detects and analyzes crucial genetic alterations, home tests are extremely limited. For the most part, they examine only a small fraction of total DNA, relying on "surrogate" criteria such as single nucleotide polymorphisms, or SNPs, some of which, when compared to SNPs in the larger population, may indicate a statistically elevated risk.

People get their test results and jump to conclusions, either assuming everything's fine, or believing they're at high risk for a disease, which may not be the case. Some will take their test reports to a doctor, who may be just as much in the dark as the patient.

# **EDUCATION IS KEY**

Blazer and her colleagues in the Division of Clinical Cancer Genomics are laboring to correct that. As director of City of Hope's Cancer Genomics Education Program, she helps oversee a multifaceted cancer genetics education initiative. What Home DNA Tests Can (and Can't) Tell You

BY ABE ROSENBERG

The program aims to give clinicians — doctors, physician assistants, nurses, genetic counselors and others — the tools and information they need to take better care of their patients. More than 1,000 medical professionals in all 50 states and 25 countries have successfully completed the program, with another 1,200 currently enrolled.

At the same time, Blazer says testing companies need to do a better job informing their customers.

"Testing companies must provide black-letter warnings that are very clear and hard to miss," she said. Blazer wants companies to offer more comprehensive resources — like guidance on where to find a qualified geneticist in your local area to receive a complete screening.

The industry is listening. Blazer chairs a direct-toconsumer working group at the National Human Genome Research Institute (part of the National Institutes of Health) that's examining existing direct to consumer information resources, and working with testing companies — including 23andMe — to improve and upgrade their offerings. Those efforts appear to be having an effect: Testing companies are adding more information to their websites and placing it more prominently.

But customers still have to read it. And once they get their test results, the next step is even more critical.

# **CONFIRM YOUR RESULTS**

"Some home tests may indicate you have a mutation associated with Alzheimer's," said Blazer, citing one example. "But it may not necessarily mean you're at high risk for the disease. There are other genetic factors involved in assessing that risk ... and those factors are not measured in a home test." That's why it's so important to follow up with testing and counseling from a health care professional who is specifically trained to administer a medically approved test and accurately interpret the results.

Why then bother with a home test at all? Blazer does see some benefit: DNA information is entering more people's comfort zones.

Not that long ago, patients would have their DNA tested anonymously, fearing discrimination in the workplace or by insurance companies if a high risk of disease were detected. The law changed in 2008, making such discrimination illegal.

"The popularity of home testing is helping to build awareness, understanding and comfort in the whole area of genetic information," Blazer said. "It's pushing the envelope, combating the fear of discrimination based on your DNA ... and it's bringing down the cost."

When more people gain more knowledge, Blazer said, it could ultimately save lives.

"I'm seeing people come forward," she said, "once they find out what they didn't know. Folks who took the test for fun, and discovered a possible risk to their health."

Just be sure to underline that word "possible."

"Remember," Blazer emphasizes, "A screening is not a diagnosis. Never take any medical action [based on a home test] without confirming the results first. The important thing to remember with direct-toconsumer tests is to get your results confirmed with a professional genetics consult."



Chandana Banerjee, M.D., M.P.A. (right), specializes in treating caregiver grief

handana Banerjee, M.D., M.P.A., had a childhood dream to become a writer or poet, and she planned on making it a career. But after getting an undergrad degree in literature, she decided to take a year or two off before going for her Ph.D. It was a decision that would change her life.

During the break, Banerjee became fascinated with health policy and marketing, so she abruptly switched course and earned a master's in public administration. Soon afterward, the future physician became director of marketing for a Medicaid company in Connecticut.

That's when an unexpected tragedy struck that rocked her personal and professional life, eventually leading her to City of Hope's Department of Supportive Care Medicine.

## **ANEW DIRECTION**

"Shortly after finishing my first year in marketing, my father, who was visiting India at the time, had an emergency hernia operation," Banerjee said. "Inadequate care by his medical team led to him being septic, and he died from cardiac arrest. His death made me realize that to really make a difference, I needed to become a clinician and work with patients directly. Palliative care was in its early phase of conception at the time, so initially, given my interest in children and underserved communities,

I decided on pediatrics."

Banerjee's experience dealing with grief shaped her career and inspired her recent article in the *Journal of Pain and Symptom Management*, "Grieving to Grieve." It's a deep dive into what she calls "anticipatory grief," a grief reaction among people who are facing the eventual death of a loved one during a terminal illness.

"Even in its silent form, grief is a powerful emotion that often plays a powerful role in shaping people's lives," she said. "My personal belief is that anticipatory grief has its various stages, much like conventional grief, and to truly address someone's feelings and help them heal, one needs to recognize the impending loss that is to occur and address a person's grief around that impending loss.

"By addressing both pre- and post-loss phases of grief, we can better understand grief in its entire spectrum, which then allows us to guide people through their healing process."

In her article, she explains how anticipatory grief affects not only families and friends of afflicted patients, but also caregivers and physicians. It is, she says, a tragically overlooked aspect of practicing medicine that needs to be addressed.

"It's well known among physicians that we are not taught the art of grieving," Banerjee said. "Only recently have medical schools started teaching medical students how to cope with emotions we face in our careers that might ultimately drain us or impact our professional and personal lives."

# **HEALING THE HEALERS**

City of Hope provides a support system with the Schwartz Center Rounds program, a series of workshops created for physicians and all employees of the medical center, clinical and nonclinical alike. They provide a safe space to explore and elaborate on issues and emotions related to daily patient care, Banerjee said.

The rounds are part of the Schwartz Center for Compassionate Healthcare, founded and named in memory of Kenneth Schwartz, a cancer patient who died from lung cancer at a very young age. He served as an inspiration for the medical center staff.

In his writings, he described that it was his caregivers' kindness that often 'made the unbearable bearable,'" said Banerjee, physician lead for Schwartz Center Rounds. "He believed that caregivers also needed to be supported and listened to as they selflessly cared for their patients."

Supporting the emotional needs of patients and their loved ones has long been an important mission at City of Hope, which recently launched the Hospice & Palliative Care Medicine Fellowship Program, a one-year fellowship intended to train physicians to specialize in hospice and palliative care — an increasingly essential complement to existing care teams.

"What is unique about the HPM program is that it's the only standalone NCIdesignated cancer center fellowship on the West Coast," Banerjee said.

The work of supportive care physicians at City of Hope has also been supported for the last 20 years by the Arthur M. Coppola family, which endowed a chair in supportive care medicine in 2008. Arthur M. Coppola was chairman and CEO of The Macerich Company, one of the country's leading developers of retail real estate. He established the chair in 2008 to recognize the importance of care that addresses the whole person and embraces the patient's family as part of the treating, healing and dying process. The current chair is William Dale, M.D., Ph.D.

# **GRAPPLING WITH GRIEF**

Banerjee's work in hospice and palliative care, as well as her personal struggle with grief, have given the doctor a deep insight into the grieving process, a

process universal to the human experience that nevertheless remains a rather taboo subject.

Being mindful of how the process works can be invaluable in charting a path to healing, she said. And it's essential that physicians recognize anticipatory grief in patients and their loved ones and

connect them with the wide range of

palliative care workers, psychiatrists,

reality of losing someone they love."

Healing from loss is a deeply personal

and expressing grief through a creative

outlet can be a powerful tool in finding

closure. After dealing with the shocking

loss of her father, Banerjee found

"While someone will take comfort

in prayer or participate in grief and

bereavement sessions, others may

writing, song or paintings," she said.

"Poetry was the form I chose to express

written poetry from a very young age, so

writing about my father's death and my

my grief when I was finally ready. I've

**Even in** connect them with the with resources at City of Hope. its silent "Our spiritual care team, social workers, form, grief psychologists and Child Life specialists will guide our families through the is a powerful emotion that process that takes many forms, she said, often plays a powerful role loss of her father, Banerjee found comfort through her love of writing. in shaping people's bereavement sessions, others ma express it in forms of meditation, writing, song or paintings," she sa "Poetry was the form I chose to express the form I chose t

Chandana Banerjee, M.D., M.P.A.

emotions in the form of verse seemed appropriate."

Regardless of which path to healing one chooses, dealing with this powerful emotion is inevitable. It is, after all, one common experience shared by all people.

"Every human being, when lost, is grieved, even the vile ones, and hence grief is what unites us, no matter how different we are as people — and how differently we choose to grieve."

# Supporting Supportive Care



ate and Arthur Coppola joined the City of Hope community in September for a special celebration of the investiture of William Dale, M.D., Ph.D., as the Arthur M. Coppola Family Chair in Supportive Care Medicine. The Coppola family established the endowed chair in 2008 to recognize the importance of care that addresses the whole

person and embraces the patient's family as part of the treating, healing and dying process.

Art Coppola, who was honored with the Los Angeles Real Estate & Construction Industries Council's Spirit of Life® Award in 2007 and have been a part of the industry group for more than a decade, served for 25 years as chairman and CEO of The Macerich Company, one of the country's leading developers of real estate.

Kate Coppola's dedication to healing extends beyond the family's philanthropy. A certified sound healer, Kate conducted a special sound bath class for patients, family and staff through the Sheri & Les Biller Patient and Family Resource Center. The ancient healing practice uses Tibetan singing bowls and other sounds to encourage meditation and reduce stress and anxiety.

Dale notes that he was drawn to City of Hope in part because of the Coppola Family Chair, which provides him with a vital and stable source of revenue for research, education and faculty support. A nationally recognized leader in creating supportive approaches to care for patients with complex health issues, especially older adults with cancer, he leads a multidisciplinary team of medical and caring professionals at City of Hope.



Celebrating the investiture of the Arthur M. Coppola Family Chair in Supportive Care Medicine in September 2018 are, from left, Tamra Dale, William Dale, M.D., Ph.D., Art Coppola and Kate Coppola.



# REMEMBERING ARTI HURRIA, M.D.

## BY SAMANTHA BONAR

The City of Hope community was devastated by the untimely death of Arti Hurria, M.D., director of City of Hope's Center for Cancer and Aging. She is survived by her husband, Thomas Lee, M.D., and her daughter, Serena, as well as her legacy at City of Hope, where she pioneered geriatric cancer care and was beloved by those who had the privilege to work with her.

"Dr. Arti Hurria was known by many and loved by all who had the pleasure to work with her," said Robert Stone, president and chief executive officer of City of Hope. "Her passion for her patients, her team and her colleagues was only surpassed by her passion for her family, especially her daughter."

"I am always cautious to use the term 'perfect' for my colleagues in academic medicine," said Sumanta Pal, M.D., co-director of the Kidney Cancer Program at City of Hope. "Some might excel in clinical medicine, but lack in research expertise — some may excel in hospital politics, but they lack interpersonal skills that guide day-to-day interactions with peers. Dr. Hurria was flawless. She was perfect in every way."

Hurria, the George Tsai Chair in Geriatric Oncology, specialized in treating cancer patients who are 65 and older. A trained geriatrician and oncologist who served fellowships at Harvard and Memorial SloanKettering Cancer Center, Hurria focused on improving treatments for older patients while minimizing side effects that could affect quality of life.

"It is almost impossible to overstate the impact Arti has had on the world of cancer and aging," said William Dale, M.D., Ph.D., the Arthur M. Coppola Family Chair in Supportive Care Medicine at City of Hope.

Hurria was a first-generation American of immigrant parents from India. Born in Brooklyn, New York, she moved with her family to Southern California when she was 8. "My parents are physicians, and when I was growing up, they were training very hard in the new medical system. So I was brought up in an environment that truly believed in the power of medicine to make a difference in the world," she shared in a 2018 interview with the American Society of Clinical Oncology.

After graduating from high school, Hurria was accepted into a



seven-year combined medical program at Northwestern University and Northwestern Medical School. She was a medical student at Northwestern when she met her mentor, Steven T. Rosen, M.D., now provost and chief scientific officer and the Irell & Marella Cancer Center Director's Distinguished Chair at City of Hope. "I was a second-year medical student and I thought I wanted to be an oncologist," she recalled in a 2017 City of Hope interview. "So, I knocked on his office door and he invited me to follow him around his clinic on Tuesday afternoons."

In 1995, Hurria moved to Boston for an internship at Beth Israel Medical Center, where she said she "fell in love" with the geriatric patient population. She completed a Harvard geriatrics fellowship to bolster her skills and knowledge in treating older patients before entering her oncology fellowship at Memorial Sloan Kettering Cancer Center.

Hurria was thrilled to become director of the newly formed Center for Cancer and Aging at City of Hope in 2006, where she served as the principal investigator on grants leading to evidence-based recommendations to improve clinical care for older adults with cancer. When she was recently named the George Tsai Family Chair in Geriatric Oncology, she told the crowd, "It's my mission, what I like to call 'the dream,' that all older adults with cancer will receive personalized, tailored care, utilizing evidence-based medicine with a multidisciplinary approach."

As an oncologist specializing in geriatric medicine, Hurria was part of a rarefied group of physicians. In the United States, there are fewer than 200 geriatric oncologists, even though 60 percent of all cancers are diagnosed in people age 65 and older.

"Historically, clinical trials have left out people who are older and more experienced, which doesn't make much sense," Hurria said. "We're changing that. Older people have much to teach us. Their bodies are different. Their lives are different."

# "There will never, ever, be anyone like her."

"There is no organization that is relevant in the field of cancer and aging for which she hasn't played a leading role. Her commitment to the field is immense," Dale said. "It is almost impossible to believe that this force of nature is gone. Her presence has been ubiquitous, and her influence on the field will be felt for many, many years. The only thing that was larger than her contributions to date was the contributions she was going to make. She had so much more to give."

Hurria had been honored with multiple awards, including the Frederick Stenn Memorial Award for Humanism in Medicine. She was awarded both the Paul Calabresi Award and the BJ Kennedy Award, the top honors in the field of geriatric oncology.

Sumanta Pal, M.D.

"At City of Hope, she was the doctor that every fellow and junior faculty clamored to work with," Pal said. "Even though I am now 10 years out of training, I still turned to her for advice. She was a mentor to mentors, if you will. And on a human level, she was a human. She was someone who cared deeply about everyone she interfaced with, whether you were her patient, her student, her secretary or even a passing acquaintance, she sincerely conveyed interest in your well-being. ...There will never, ever, be anyone like her."



Nearly four decades ago, newspapers across the nation heralded the development of bacteria-created synthetic human insulin. The breakthrough was based on technology created by City of Hope's Arthur Riggs, Ph.D., the Samuel Rahbar Chair in Diabetes & Drug Discovery, and Keiichi Itakura, Ph.D. (see page 16) Please join transplant patients, donors, families and friends for a

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# Turns out you don't have to be a doctor to cure cancer.

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