City of Hope®

CITY NEWS

VOL. 30 NO. 3 FALL 2019

Within Our Grasp

A dream team of diabetes researchers sets its sights on a cure

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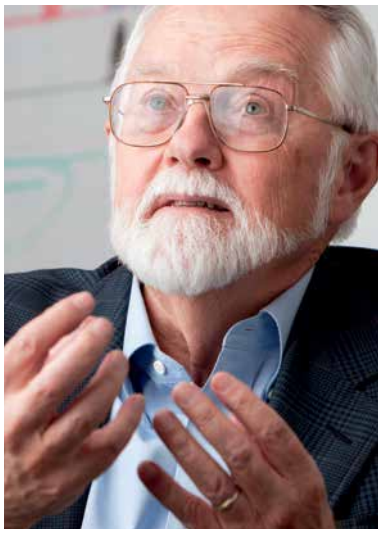
CITY OF HOPE IS OBSERVING NATIONAL DIABETES MONTH

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.

City News is published quarterly for donors, volunteers and friends of City of Hope.



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INSIDE THE QUEST TO CURE TYPE 1 DIABETES

For more than 100 years, City of Hope has tackled some of the toughest diseases plaguing humankind. Today, we are recognized as a premier cancer center renowned for our leadership in swiftly advancing discoveries to benefit patients around the globe.

Since November is National Diabetes Month, we also recognize our pioneering work in diabetes research. At City of Hope, the fields of cancer and diabetes are inextricably linked. Many of our diabetes scientists work in cancer research, and our cancer researchers develop ideas that inspire breakthroughs in diabetes. The cross-pollination leads to a geography of innovation, and new paths in prediction and prevention.

In this issue of City News, we shine the light on our pursuit of a cure for type 1 diabetes and the implications of our type 1 research for treatment of type 2 diabetes. The potential impact is tremendous – types 1and 2 diabetes impact the lives of more than 422 million people worldwide, according to the World Health Organization.

Our scientists have revolutionized the understanding and treatment of the disease, and we are driving exciting developments in cell transplantation, gene regulation, immune tolerance and the systemic understanding of diabetes as a complex, multifaceted disease.

Thanks to your support, we are moving quickly to innovate, accelerate and translate strategies to catalyze a new era of breakthrough discoveries. We are grateful for your generosity and partnership in making hope a reality.

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

cityBUZZ

Songs of Hope

Songs of Hope is a unique evening honoring songwriters and composers, with live music and a silent auction. The event brings together more than 300 music industry celebrities and professionals, and to date has raised over $3.4 million for City of Hope.

A-list celebrities mingle with A-list scientists at the annual Songs of Hope event

newHOPE

NEW FACES • ADVANCING SCIENCE • BEGINNINGS

Anna Wu, Ph.D.

Anna M. Wu, Ph.D., is professor and chair of the Department of Molecular Imaging & Therapy, professor in the Department of Radiation Oncology and co-director of the Center for Theranostic Studies within the Diabetes & Metabolism Research Institute at City of Hope. She also holds the title of research professor in the Department of Molecular and Medical Pharmacology at the David Geffen School of Medicine at UCLA. She is a past chair of the California Breast Cancer Research Council, and fellow and past president of the World Molecular Imaging Society.

Wu is the co-founder and chief scientific adviser to ImaginAb Inc., an L.A.-based startup that develops and commercializes engineered antibodies for clinical imaging in cancer and other diseases. Wu began her independent research career as an assistant research scientist at Beckman Research Institute of City of Hope and advanced to the position of professor of molecular biology in 2002. She received her bachelor's degree in biochemical sciences from Harvard University and a Ph.D. from Yale University in molecular biophysics and biochemistry.

Investiture Highlights

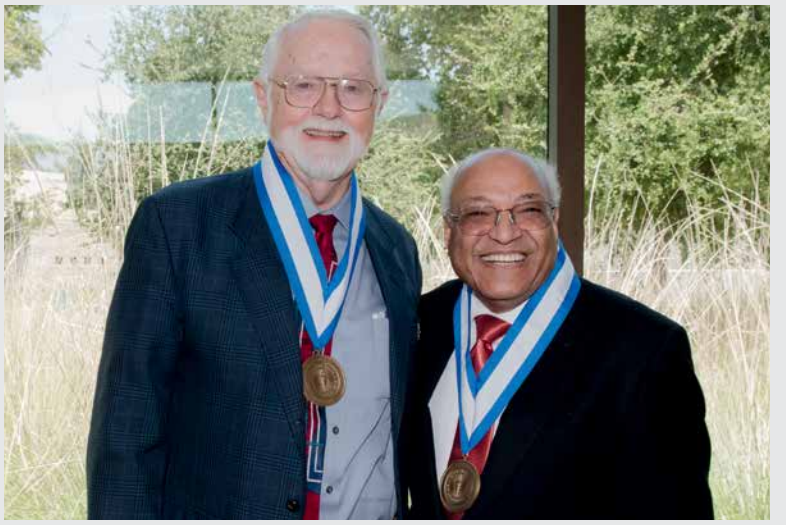
Fouad Kandeel, M.D., Ph.D.

After 20 years of unwavering friendship, countless scientific discoveries and life-changing contributions to City of Hope, some call the bond between Fouad Kandeel, M.D., Ph.D., and Arthur Riggs, Ph.D., dynamic and powerful, and they are not wrong. It seemed only fitting that Kandeel was honored as the inaugural recipient of the Arthur D. Riggs Distinguished Chair in Diabetes & Metabolism Research.

Kandeel is professor and chair of the Department of Clinical Diabetes, Endocrinology & Metabolism and chair of the Department of Translational Research & Cellular Therapeutics, as well as associate director of the Diabetes & Metabolism Research Institute at City of Hope. Riggs is the Samuel Rahbar Chair in Diabetes & Drug Discovery and director of the Diabetes & Metabolism Research Institute, marking his 50th year at City of Hope. Kandeel joined City of Hope in 1991.

"Dr. Kandeel is a gifted and accomplished clinician and researcher, whose leadership in diabetes, thyroid cancers and neuroendocrine disease is helping us translate revolutionary discoveries into life-changing treatments," said City of Hope President and CEO Robert Stone.

Kandeel has accomplished an extraordinary amount since he has been here, including developing the Diabetes and Cardiovascular Risk Reduction Program in 1992, serving on the National Cancer Comprehensive Network for thyroid cancer and for neuroendocrine tumors since 1999, and establishing the Levine-Riggs Diabetes Research Symposium in 2000.



Fouad Kandeel, M.D., Ph.D. (right), with Arthur Riggs, Ph.D.

Kandeel led efforts to create an islet processing facility at City of Hope, which has provided national distribution of islets and garnered multiple grants from the National Institutes of Health and JDRF.

"It is verifiably the best and largest islet preparation and distribution program in the country," Riggs said.

As director of the Islet Cell Transplantation Program, Kandeel has been the driving force in bringing this revolutionary treatment for type 1 diabetes to City of Hope since 2000.

Within Our Grasp

BY WAYNE LEWIS

A dream team of diabetes researchers, supported by a family that shares its vision, sets its sights on a cure

Learn more about City of Hope's history of diabetes innovation

The staff of the Diabetes & Metabolism Research Institute at City of Hope

Discovering insulin's role in processing sugar. Identifying a blood factor that serves as a marker for glucose control. Creating technology leading to the development of synthetic human insulin.

For nearly 50 years, scientists who have made major advances in the understanding and treatment of diabetes have called City of Hope home.

"I don't think anyone else in the country has made as many contributions to diabetes research as the scientists at City of Hope," said Arthur Riggs, Ph.D., Samuel Rahbar Chair in Diabetes & Drug Discovery, who co-led the investigations that resulted in synthetic human insulin.

> "This is an integrated way to treat."
>
> Fouad Kandeel, M.D., Ph.D.

That history is part inspiration and part prelude for today's City of Hope diabetes researchers. Building on past milestones, as well as the institution's acute understanding of the role of the immune system in cancer, investigators work on an integrated approach to type 1 diabetes with the support of many donors, including the transformative leadership gift that established The Wanek Family Project for Type 1 Diabetes.

"Because they gave so generously, the Waneks allowed us to try some approaches that otherwise would not have been funded," said Bart Roep, Ph.D., the Chan Soon-Shiong Shapiro Distinguished Chair in Diabetes and director of The Wanek Family Project. "What I like most is that they have the same ambition as I, which is to cure diabetes and do it quickly. That focus helps us cut to the chase and be very patient-minded."

City of Hope's strategies for fighting type 1 diabetes center on three key features of the disease: dysfunction in the insulin-producing beta cells of the pancreas, the immune system's role in attacking those cells, and potentially deadly complications. These efforts span a host of disciplines, uniting basic and clinical science.

NEGOTIATING WITH THE IMMUNE SYSTEM

City of Hope has been a pioneer of an investigational procedure called islet cell transplantation since 2004. The therapy takes donated beta cells, found in mini-organs known as islets, and implants them in type 1 diabetes patients in a bid to kick-start insulin production.

While City of Hope researchers advanced that treatment, the institution built up expertise in other areas.

"As we established the islet cell transplantation platform, it became natural that we look at ways of focusing on immune modulation strategies," said Fouad Kandeel, M.D., Ph.D., the Arthur D. Riggs Distinguished Chair in Diabetes & Metabolism Research, who directs City of Hope's Islet Cell Transplantation Program.

Today, researchers at City of Hope are hard at work on an array of therapies that tackle the immune component of type 1 diabetes. This direction requires nuance to quiet the immune assault on beta cells without compromising the body's natural defenses against threats such as invasive microbes.

"What we try to do at City of Hope is not bombard the immune system into submission, but negotiate with it," said Roep, who also is professor and founding chair of the Department of Diabetes Immunology. "We try to teach the immune system to preserve beta cells."

Approaches include a "reverse vaccine" close to being tested in clinical trials, potent designer antibodies and the newest generation of CAR T therapy.

RARE COMBINATIONS

Meanwhile, City of Hope investigators delve into the molecular mechanisms behind beta cell health. They are developing ways to revitalize beta cells and buttress them against immune attack, with efforts that extend to growing new cells in the lab to augment a limited stock of human islets.

The signature spirit of collaboration at City of Hope leads to promising combinations such as Roep's work with Debbie Thurmond, Ph.D., the Ruth B. & Robert K. Lanman Chair in Gene Regulation & Drug Discovery Research.

"There aren't a lot of examples of a beta cell biologist and an immunologist working closely together on a project that has a direction forward," said Thurmond, who also is professor and founding chair of the Department of Molecular & Cellular Endocrinology. "He and I both recognize that individually our research is unlikely to cure the disease, but together we can probably design some very creative solutions that we hope will be maximally effective."

MOVING SIDE EFFECTS TO THE CENTER

Many know about the day-to-day burdens faced by type 1 diabetes patients, such as the need to monitor blood glucose and inject with insulin. But it is the complications of the disease — including kidney failure and blindness — that endanger lives and erode quality of life.

"Once insulin became freely available, nobody really needed to die of diabetes. What kills patients is the complications associated with diabetes," said Rama Natarajan, Ph.D., who first established the link between complications and epigenetics — that is, changes in gene expression due to external or environmental factors.

Natarajan is City of Hope's National Business Products Industry Professor in Diabetes

Research and professor and chair of the Department of Diabetes Complications & Metabolism. She and her colleagues are creating new knowledge about the underlying mechanisms behind complications of the disease while developing potential treatments. Their studies are accelerated by recent advances in technology that allow for unprecedented views into basic processes.

"By looking deeper into the genome and epigenome using these amazing technologies, we are seeing so many new aspects of type 1 diabetes that we never did before," Natarajan said.

THE POTENTIAL OF PRECISION MEDICINE FOR DIABETES

City of Hope's integrated approach suggests a vision for the future of type 1 diabetes care — one where there is a therapy appropriate for every patient. The mix of cellular therapies that renew and protect beta cells, immunotherapy, islet cell transplantation and treatments for mitigating complications could be adjusted to the needs of each case.

"This is an integrated way to treat," said Kandeel, who also is associate director of the Diabetes & Metabolism Research Institute at City of Hope and chair of the departments of Clinical Diabetes, Endocrinology & Metabolism and of Translational Research & Cellular Therapeutics. "It is also a form of precision medicine, giving the patient exactly what they need."

To realize that vision requires close connections between basic research and clinical science — which also makes the institution a haven for top scientists.

"The advantage to working at City of Hope is that I'm encouraged to have intellectual curiosity, but I'm also provided with the means and the colleagues to see that the work comes to fruition in clinical care," Thurmond said. "It's the best of both worlds."

LINKS TO OTHER DISEASES

Many of the breakthroughs in type 1 diabetes from City of Hope research also represent progress against type 2 diabetes; at the same time, type 2 diabetes is an area of focus for many investigators in the Diabetes & Metabolism Research Institute.

"I don't like saying 'type 1 diabetes research.' I prefer the more general 'diabetes research,'" said Riggs, director of the Diabetes & Metabolism Research Institute. "Insulin is important to both types, the loss of beta cells is a critical aspect in both, and the complications are more or less the same."

Likewise, City of Hope's excellence in cancer care presents a boon to efforts against type 1 diabetes.

After all, many of the researchers describe the diseases as flip sides of the same coin. Cancers develop after the immune system has failed to root out abnormal cells; in type 1 diabetes, the immune system is overactive in attacking beta cells.

"We have a unique opportunity to be at the forefront of investigating the interface between cancer and diabetes," Riggs said.

Indeed, some diabetes investigations take cues from certain aspects of cancer studies, and vice versa. And while City of Hope does not treat a large number of diabetes patients, a small portion of cancer patients develop type 1 diabetes as a side effect of treatment, and they receive high-quality care from City of Hope endocrinologists.

With a distinguished history behind them and promising projects in progress, City of Hope researchers are cutting a path to type 1 diabetes breakthroughs — and one day, perhaps soon, a cure.

Personal Giving, Global Impact

The National Business Products Industry (NBPI) has been a reliable supporter of City of Hope's mission for 37 years, raising an astonishing $200 million for cancer and diabetes research since 1983. Comprising corporate leaders in a variety of global industries, the NBPI's ambitious philanthropic effort has funded numerous facilities around the City of Hope campus — the Center for Biomedicine & Genetics, the Arnold and Mabel Beckman Center for Cancer Immunotherapeutics & Tumor Immunology, City of Hope Helford Clinical Research Hospital, the Chemical GMP Synthesis Facility — as well as basic research to help new talent acquire grants.

In 2011, the National Business Products Council for City of Hope was looking for a targeted challenge in a new area and landed on diabetes, raising $1.25 million through a three-year personal giving program to endow the National Business Products Professorship in Diabetes Research held by Rama Natarajan, Ph.D., a leader in the search for a diabetes cure for 30 years. Professor and chair of the Department of Diabetes Complications & Metabolism at the Diabetes & Metabolism Research Institute, Natarajan runs a lab devoted to understanding the molecular mechanisms and mutations behind the acceleration of complications from diabetes, as well as the persistence of "metabolic memory" that results in long-term dysfunction at the epigenetic level even after a patient has made essential lifestyle changes. Her research may lead to key insights about stopping and reversing the harmful effects of the disease, including cognitive decline.

The NBPI's member companies are all international entities, and since diabetes affects hundreds of millions of people around the world, supporting Natarajan's important work has the potential to make a substantial impact globally. The annual *Spirit of Life®* gala that took place in September in Chicago celebrated an incredibly fruitful relationship that the NBPI and City of Hope expect to grow in ever more meaningful ways.

Ancient Genes, New Treatments

Proteins with a long biological history could play a key role in metabolism

BY WAYNE LEWIS

Debbie Thurmond, Ph.D., studies proteins that have a long biological history. "They're an old gene family, ancestral," said Thurmond, holder of City of Hope's Ruth B. & Robert K. Lanman Chair in Gene Regulation & Drug Discovery Research and member of The Wanek Family Project for Type 1 Diabetes. "They're in virtually every cell. Flies, worms and yeast all have them."

Hear more from Debbie Thurmond, Ph.D.

Crucial to survival, the family of SNARE proteins are an essential part of the body's complex transport system, helping to regulate diverse biological processes.

Thurmond investigates the role that certain members of that family play in metabolism — research that has the potential to result in new therapies for type 1 diabetes. And what she and her colleagues learn has implications for treating type 2 diabetes as well.

PROVERBIAL SHIELD

For the cell biologist, it starts with the health of insulin-producing beta cells, found in mini-organs called islets located in the pancreas. In type 1 diabetes, the immune system kills off beta cells, and her research points to a way to defend them.

"In the context of type 1 diabetes, we're trying to keep the cells functioning, and we're trying to put a proverbial protective coating over them," said Thurmond, who also is founding chair of the Department of Molecular & Cellular Endocrinology and a professor in the Diabetes & Metabolism Research Institute at City of Hope.

Thurmond's research group has found that one particular SNARE protein, called syntaxin 4 or STX4 for short, is suppressed in type 1 diabetes. Inversely, they also have identified STX4 as a factor that can preserve the body's own beta cells and deter the onset of the disease.

The team is pushing forward lab studies into technologies that use the protein's power in order to treat type 1 diabetes. Building on a potential gene therapy platform that could stimulate the body to produce STX4, they are working on a cellular therapy that interferes with signaling that suppresses the protein.

THE POWER OF COLLABORATION

Although the prospective therapies hold promise, Thurmond is aware that in type 1 diabetes, one must still contend with the autoimmune attack. So she has joined forces with Bart Roep, Ph.D., director of The Wanek Family Project, the Chan Soon-Shiong Shapiro Distinguished Chair in Diabetes, and professor and founding chair of the Department of Diabetes Immunology at City of Hope.

Together, the researchers are developing a combination treatment: Thurmond's technology for stimulating STX4 plus Roep's "immunosuppression-lite." (Strong suppression of the body's natural defenses would sabotage diabetes patients' ability to ward off dangerous microbes and other threats.)

"Short-term in the lab, we can protect beta cells from immune attack with my technologies," Thurmond said. "But when the immune system kicks into high gear, we're guessing it's probably going to be insufficient. Bart is really good at finding ways to 'negotiate with the immune system,' as he phrases it. The hope is that this will be a sustainable strategy for type 1 diabetes."

CROSSING OVER

Fortunately, Thurmond's approach also may provide an answer to type 2 diabetes, which is characterized by malfunctioning beta cells, as well as tissue in the body becoming insensitive to insulin.

"STX4 can resurrect a dying type 2 diabetic human islet," she said. "That's what I would consider a great therapeutic target."

Because STX4 and related proteins fulfill numerous roles within the body, they are sometimes referred to as "multitaskers." A second function of STX4 makes it especially promising for treating type 2 diabetes: It aids the body's skeletal muscles in absorbing sugar, helping to reverse insulin resistance.

> "STX4 can resurrect a dying type 2 diabetic human islet."
>
> Debbie Thurmond, Ph.D.

A 2015 laboratory study by Thurmond and colleagues highlighted some eye-opening possibilities. The scientists altered mice to overexpress STX4 in both the pancreas and the muscles. The difference was dramatic. The mice showed neither damaging effects from a high-fat diet nor age-induced insulin resistance. Though they grayed and gained weight in old age, they stayed livelier and lived far longer than their peers in the control group.

"People looked at the gene we focused on and said, 'This has no implications in aging,'" Thurmond said. "But it does in metabolism. When you improve blood sugar control, you are improving aging."

Further experiments helped to tease out the positive effects of STX4's role in beta cells versus muscle cells.

"The answer is, it's both," she said. "That's why we work on multitaskers."

To go from discovery to application, Thurmond is seeking the best way to deliver STX4 in the body. With its numerous functions, the protein might have negative effects if overexpressed systemwide. Thurmond plans to run an expansive set of tests to see how STX4 affects a variety of different cell types. The answers she finds ultimately could bring good news to people who face type 2 diabetes.

"There's a lot of work to be done, but I'm very optimistic," she said.

Kindred Spirits in the Quest for Innovation

Lions Clubs International (LCI) has been an active supporter of City of Hope's mission for over 60 years, but the volunteer humanitarian organization has never stopped looking for new ways to contribute. Recently, as part of a new commitment to combat diabetes globally, LCI launched an ambitious Diabetes Innovation Fund at City of Hope to raise $1 million for advancing research into preventing and treating the growing disease. Diabetes is a core area of focus for the Lions and City of Hope has remained an established, approved fundraising partner for LCI.

For the Lions, the effort fits easily into the group's larger historical purpose.

"Ever since our affirmative response to a plea from Helen Keller in 1925, the legacy service focus of Lions Clubs International and its 1.4 million members has been to serve the needs of the blind and visually impaired," said Robert Stewart, immediate past council chair, California Lions (Multiple District Four), LCI. "Diabetes is a leading cause of blindness, and diabetes is a worldwide epidemic. City of Hope is leading the medical research effort to stamp out diabetes 1 and 2. We share the same goals."

The Diabetes & Metabolism Research Institute at City of Hope is already hard at work investigating how diabetes develops and searching for new ways to prevent and reverse it using novel immunotherapy approaches and beta cell transplantation. The innovation fund will augment these lifesaving efforts, extending a fertile relationship that has already resulted in LCI's funding of the Family Center and the Japanese Garden on the City of Hope campus. But this is not just a philanthropic partnership; many Lions members are grateful for the treatment they've received as patients at City of Hope. To show its gratitude for LCI's support, City of Hope will host the 63rd annual Lions Tribute Day in March 2020.

"We see the Lions partnership with City of Hope as one of kindred spirits, a symbiotic relationship," said Stewart. "The Lions service contribution throughout California, all 20,000 of us, includes inspired engagement with our communities in promotion of and financial assistance to City of Hope. We are in this together."

The Missing Link

A new study by John Termini, Ph.D., digs into the genomic links between the two disorders

BY ZEN VUONG

Higher than normal blood sugar levels are linked to more DNA damage that is repaired less often in the body's cells, which could explain why people with diabetes have an increased risk of developing cancer, according to ongoing research led by City of Hope.

Click here to read more online.

Human kidney cells stained to reveal DNA damage induced by elevated glucose (green dots).

Such genomic instability can cause and promote the progression of cancer, said John Termini, Ph.D., professor in the Department of Molecular Medicine.

"As the incidence of diabetes continues to rise, the cancer rate will likely increase as well," Termini said. "In an ironic twist of fate, some cancer treatments increase the risk of diabetes, which in turn increases the risk of cancer. The destructive machine feeds itself. That's why City of Hope — best known for its leading-edge cancer therapies — has also taken on the challenge of finding a cure for diabetes."

SIMILAR RISK FACTORS

The diabetes and cancer link has been discussed in scientific circles for years; however, researchers are still searching for the disease-causing catalyst. This research may bring us one step closer to finding it. Termini presented his ongoing research at the American Chemical Society (ACS) Fall 2019 National Meeting & Exposition on Aug. 25 in San Diego. He elaborated on early findings at an ACS press conference on Aug. 26.

The link between diabetes and certain cancers may be due, in part, to shared risk factors such as aging, obesity, increased inflammation, dietary choices and inactive lifestyles. People with type 2 diabetes (the most common form) are 2.5 times more likely to develop liver or pancreatic cancer. They also run a higher than normal risk of developing colon, bladder and breast cancer. Diabetic women with breast cancer have a higher mortality rate than women with breast cancer alone.

Conversely, some forms of chemotherapy induce insulin resistance, bringing on diabetic symptoms. Immunotherapy, one of the most exciting advances in cancer treatment, may bring on the less common type 1 diabetes, which is essentially an autoimmune disorder. With immunotherapy, the body's immune system is "unleashed," and it may attack critical insulin-producing cells in the pancreas.

> "As the incidence of diabetes continues to rise, the cancer rate will likely increase as well."
>
> John Termini, Ph.D.

Termini and his colleagues showed, in tissue culture and diabetic mouse models, that elevated glucose increased the presence of DNA adducts — chemical modifications of the DNA. Specifically, they found that a DNA adduct called N2-(1-carboxyethyl)-2′-deoxyguanosine, or CEdG, occurred more frequently in diabetic models than in normal cells or mice. Moreover, high glucose levels increased DNA strand breaks and interfered with DNA repair, which is required for removal of CEdG. The result is genome instability that could cause cancer.

Recently, Termini and colleagues completed a clinical study that measured the levels of CEdG and its RNA counterpart (CEG) in people with type 2 diabetes. People with diabetes had significantly higher levels of both CEdG and CEG than people without the disease.

The scientists identified two proteins that appear to be involved: transcription factor HIF1α and signaling protein mTORC1, both of which are less active in people with diabetes. HIF1α activates several genes involved in the repair process. The scientists found that if they stabilized HIF1α in a high-glucose environment, they increased DNA repair and reduced DNA damage. The protein mTORC1 controls HIF1α, so if mTORC1 is stimulated, then HIF1α is stimulated, Termini said.

METFORMIN MAY REDUCE CANCER RISK

In theory, a medication that lowers blood sugar levels in diabetics could also potentially fight cancer by "starving" malignant cells to death. Evidence exists showing that diabetics who take metformin, the No. 1 drug for treating type 2 diabetes, may be less likely to develop cancer. Moreover, if they contract cancer, they are significantly less likely to die from it.

"Metformin helps lower blood glucose levels and stimulates DNA repair," Termini said. "We're looking to test metformin in combination with drugs that specifically stabilize HIF1α or enhance mTORC1 signaling in diabetic animal models."

Seeking Breakthroughs at the Crossroads of Diabetes and Cancer

From common risk factors to similar treatment options, cancer and diabetes have an intimate, complex relationship, and City of Hope researchers in each field are uniquely positioned to share their expertise with each other. To support this fruitful dialogue, the Alfred Mann Foundation has endowed the Alfred E. Mann Chair in Cancer and Metabolism, which will allow a City of Hope scientist to lead a new department dedicated to exploring the intersection between cancer and metabolic disorders such as diabetes.

"The endowment is helping us build a new division that will be dedicated to coordinating, leveraging and extending City of Hope's expertise in these two main areas of institutional priority," said Anoosheh Bostani, chief financial officer af the Mann Foundation.

"Facilitating breakthroughs that lead to practical advances in the fight against cancer and diabetes honors the passion for discovery Alfred E. Mann championed his entire life."

Mann was a serial entrepreneur who started and sold numerous companies, many of which were focused on breakthrough medical technology. As a member of the National Academy of Engineering with several degrees in physics from UCLA, Mann forged new ground in biomedical business development that led to the creation of the insulin pump, the retinal implant and the rechargeable pacemaker. Two diabetes-focused companies he founded and chaired, MiniMed Inc. and MannKind Corporation, developed glucose monitoring systems and inhalable insulin, along with other novel therapeutics and drug delivery tech for the treatment of both type 1 and type 2 diabetes.

In 1985, Mann launched his nonprofit foundation, which is devoted to funding practical innovations in medical devices designed to help patients with underserved conditions. He was chairman of the foundation's board of trustees for 21 years. Mann died in 2016 at the age of 90, but the pioneering research he always encouraged will continue on through his forward-thinking foundation.

"As a businessman and as a philanthropist, Mr. Mann dedicated himself to finding solutions that make life better for those suffering from health and medical issues." said Bostani. "We can think of no better way to extend his legacy of hope and discovery than by supporting City of Hope's vital mission."

When It's Personal

The City of Hope diabetes researchers who struggle with type 1 diabetes themselves

BY ABE ROSENBERG

Jeannette Stratton

Among the many talented diabetes researchers at City of Hope, there are several for whom the mission is deeply personal because they are type 1 diabetics themselves. Here are a few of their stories.

Click here to read more online.

JEANNETTE STRATTON: "I CRIED LIKE A BABY"

At the slightest urging, Jeannette Stratton rattles off a list of the many type 1 diabetes research projects at City of Hope. A self-described "nerd," she comes across as an authority on the disease, as well as someone familiar with every inch of the Duarte, California, campus.

She is both.

At City of Hope for nearly two decades, Stratton does one of those "keep-the-wheels-turning" jobs. As administrative program manager for the Islet Cell Transplantation Program, Stratton writes grant applications, crafts protocols, handles regulatory paperwork and maintains reams of data for each patient, tracking their progress.

Her formidable skills took something of a back seat, however, when she wrote her public (LinkedIn) profile:

"I am a type 1 diabetic with a biological science background and extensive clinical research experience."

Why mention type 1 diabetes first?

"It's something I have to think about every moment of every day," she said. "I'm inseparable from it."

She was 18 and in college when she found out.

"I was overconfident," she recalled. "I figured I could easily control my blood sugar, do the injections. Basic math, right?"

A few near-death experiences convinced her otherwise.

"I had many problems the first five years. Several times I had to be rescued because my blood sugar dropped so low, I fell unconscious."

Things improved after Stratton was fitted with an insulin pump, but the learning curve was steep for the entire family, none of whom had any experience with type 1 diabetes.

Then, in a bizarre twist, Stratton's mother was diagnosed with the same illness. Mom took it in stride.

"Now we call daily to check in on each other," Stratton said. "We joke about it and move on. We have a friendly competition where we compare our quarterly A1c results and see who 'won.'"

As an administrator, Stratton doesn't interact directly with study patients, but bonds with them nonetheless through their data. She sympathizes with their blood sugar management struggles before transplant and celebrates each milestone they achieve after.

And she remembers the first one: the first successful islet cell transplant, after four years of hard work building the program.

"I was preparing a graph" showing how the patient — so sick pretransplant she'd had multiple car accidents caused by low blood sugar — was now off insulin and no longer needed it. "When we plotted her blood sugars and showed how drastically they fluctuated before transplant and how stable they became after, it really hit home." Suddenly Stratton realized what was possible.

"I wept at my desk," she remembered. "I cried like a baby."

Patrick Fueger, Ph.D.

PATRICK FUEGER, PH.D.: "I KNEW I HAD IT"

It's an unusual club, to say the least.

Patrick Fueger was 12 when he was diagnosed with type 1 diabetes.

He wasn't surprised. He'd seen it before.

"I knew I had it," he recalled. He recognized the symptoms: fatigue, thirst, multiple bathroom breaks. It was all very familiar. His older brother had been diagnosed a few years earlier.

"I hid [the symptoms] from my parents," he said. "I didn't want to tell them. I saw what my brother's illness did to the family. Everything changed. All the yummy food was taken out of the house. It was annoying!"

Also annoying: all the well-meaning, insensitive remarks.

"People started asking, 'Did you eat too much candy?' or, 'Will I catch it from you?'" he remembered. "Plus everybody became self-appointed endocrinologists, shouting 'Don't eat that!' all the time."

And diabetes wasn't through with the Fueger family.

Eight years later, Fueger's younger brother became the third sibling to develop the disease.

"When he was little, he would always say he wanted to get diabetes, just like us," Fueger said. "He wanted to be part of the club."

Eventually, the bonding for all three brothers did come: at special summer camps established for children with diabetes, where, instead of being known as "the sick ones," kids are able to concentrate on being kids.

Meantime, an idea was beginning to percolate in Fueger's mind.

"They put you in the hospital right away [when you're first diagnosed] to teach you how to manage your diabetes," he said. "I was in a ward with lots of other kids, some with diabetes, some with cancer, some much sicker than I.

"It gave me perspective. I felt a need to help somehow."

Sampath Rangasamy, Ph.D.

He set out to become a pediatric oncologist, but along the way several professors took note of his inquisitive nature and steered him toward research.

"I realized I could investigate the science of diabetes," he said.

These days, as associate professor in the Department of Molecular & Cellular Endocrinology, Fueger digs into the mechanics of islet beta cell biology, pursuing more eureka moments, like the likelihood that type 1 and type 2 diabetes may have more in common than once thought.

He's also focused on the metabolism of fatty liver disease, which he calls "a ticking time bomb, especially for people with diabetes.

"Half of all Americans have too much fat in their liver, putting them at risk for liver cancer, which is very tough to treat. Understanding its metabolism may help us prevent it."

To aid in that understanding, Fueger founded and directs City of Hope's Comprehensive Metabolic Phenotyping Core, where lab animals' body composition and metabolism can be measured with unprecedented precision. This includes an assay for "in vivo" (or "live") beta cell function not found anywhere else on the West Coast.

Complex work for sure, but Fueger relishes it, and he always remembers what it's for. He keeps his brothers updated and he stays in touch with old camp friends. What does he tell them?

"There are a lot of people working really hard, day and night, to try and get rid of this disease."

SAMPATH RANGASAMY, PH.D.: "I CAN'T TELL WHAT LIFE WOULD BE LIKE"

After living some 30 years with type 1 diabetes, TGen researcher Sampath Rangasamy, Ph.D., looks forward to the day when his disease is eradicated, though he can't quite grasp what that means.

"If we get a cure, oh my God!" he exclaimed. "I can't tell what life would be like!"

As a child in rural India, Rangasamy dreamed of becoming a farmer.

But when he was in middle school, the telltale symptoms of diabetes began showing up, and one day he fell into a coma. His father rushed him to the hospital on the back of his motorcycle.

Suddenly Rangasamy was very ill, and very different. Type 1 diabetes is rare in India, and until recently it carried a social stigma. Rangasamy's parents kept their son's condition a secret while he struggled to hide it from his schoolmates.

"Looking back I can't believe I did that," he said. "Somehow I managed. But it was a very stressful time."

Adding to that stress was the lack of appropriate tools: no glucose meters or insulin pumps, and the only available insulin was animal-based. Rangasamy developed serious allergic reactions.

And his career plans changed.

"I decided I need to become a doctor and cure this," he said.

His many hospital stays depressed his grades and put medical school out of reach, but Rangasamy embarked on a self-teaching binge, learning everything possible about type 1 diabetes.

A couple of decades and two Ph.D.s later, Rangasamy is immersed in the genetic sources of a daunting complication of diabetes: diabetic retinopathy, which can cause blindness. The National Institutes of Health has awarded City of Hope affiliate TGen a $2.8 million grant to identify genes associated with the condition and establish a molecular profile that can predict the severity and treatment of the disease.

He knows he's searching for his own sake.

"I've been lucky so far," he said. "I'm in good health. But the longer you live with type 1 diabetes, the greater the risk of complications. Within 15 years, the majority of type 1 patients develop retinopathy."

But Rangasamy is optimistic.

"I strongly believe we'll find a cure."

Rising Stars

New diabetes researchers bring diverse backgrounds, fresh perspectives

BY ABE ROSENBERG

They come from Amritsar, India; Beijing, China; Circle Pines, Minnesota … and lots of places in between.

Click here to read more online.

From left to right: Sangeeta Dhawan, Ph.D.; Dustin Schones, Ph.D.; Zhen Chen, Ph.D.

They are the next generation of diabetes researchers at City of Hope, bringing youthful drive and enthusiasm to our mission to eliminate type 1 diabetes once and for all.

SANGEETA DHAWAN, PH.D.: "WHAT GOES WRONG?"

What do silkworms and fruit flies have to do with diabetes?

Plenty, it turns out, if you're a young researcher with an intense curiosity plus a desire to benefit the world.

From her earliest days in India, Sangeeta Dhawan, Ph.D., wondered about the way cells behaved. The child of two doctors, her home environment fueled her inquisitiveness. "Mom and Dad would always be teaching me about science," she recalled.

> "Being near patients has totally changed the way I think about my work."
>
> Dustin Schones, Ph.D.

As she studied those intriguing insects during her doctoral program, Dhawan realized two things.

"I discovered that molecular pathways tend to be common among different organisms," she said. "And I knew that I wanted to work with cells in a way that would help people."

She found her own pathway in the study of diabetes and the mechanics of insulin-producing beta cells.

"Beta cells are the center of our health and well-being," she said. "It's an exciting field."

Most exciting is her search for the "switch": unique mechanisms that control beta cell formation, as well as when they begin secreting insulin in response to food — and why, sometimes, they stop.

In other words, she asks, "What goes wrong?"

Immediately after birth, "beta cells duplicate very rapidly," she explained, "but at this stage, they don't know how to function. They cannot sense the changes in blood sugar levels.

"Adult beta cells, on the other hand, know how to function, but they duplicate minimally. Why?"

Understanding this delicate balance is key, Dhawan said, to developing more efficient ways to rapidly grow functioning beta cells for transplant, as well as to possibly reactivate a diabetic's remaining beta cells that have gone dormant. Her work focuses on gene regulation that guides this balance.

At City of Hope since 2017, Dhawan delights in contributing to its fast-growing diabetes research center, and working alongside internationally renowned researchers like Arthur Riggs, Ph.D., the Samuel Rahbar Chair in Diabetes & Drug Discovery, whose pioneering work inspired her to study the underpinnings of gene regulation.

"The long history of breakthroughs in diabetes research at City of Hope is like a beacon to me," she said.

ZHEN BOUMAN CHEN, PH.D.: IN THE FAMILY

Raised in China, Zhen Bouman Chen, Ph.D., began studying English in third grade. She made friends with visiting American scientists in medical school, and worked with one from Riverside, California, when he set up a lab in Beijing.

Then there's the family element.

"My mom has type 2 diabetes," she explained. "And she had breast cancer."

Chen remembers a difficult two-week period during graduate school when she juggled her teaching and research while accompanying her mother to daily postsurgery radiation treatments "in a quiet basement" of a Beijing hospital.

She joined City of Hope in 2016, where she focuses on the damage wreaked by diabetes on the body's vascular system.

"It's what people suffer [from] the most," she pointed out.

Diabetics may face a variety of vascular problems ranging from peripheral artery disease to neuropathy (loss of sensation in the feet) to strokes. Chen searches for strategies to protect the blood vessels while also investigating ways to reverse damage already done.

She believes the damage may begin with the body's endothelial cells — a thin layer of cells that line the blood vessels throughout the circulatory system. They perform many functions, from filtering impurities to preventing blood clots and inhibiting inflammation. Too much glucose may impair these cells from doing those critical jobs.

Chen is applying leading-edge computational and biological tools to map the inner workings of endothelial cells.

To better understand how and why diabetes begins, Chen is also taking a close look at noncoding RNA, or RNA molecules transcribed from DNA that do not express proteins.

"For over 100 years, we've focused on genes that express proteins," Chen explained. "But 98% of our genes don't, and very little is known about them." What is known is that noncoding RNAs perform a variety of regulatory functions in the body. Chen believes there are important clues to be discovered.

"We should target the noncoding region," she declared. "It may contain the answers."

DUSTIN SCHONES, PH.D.: "I LIKE SOLVING PUZZLES"

Dustin Schones is driven by a love for science implanted at an early age. "I come from a family of educators, so a career in scientific research is not too far off the path," he said.

His path at City of Hope involves the study of obesity and how it contributes to several long-term diseases, including diabetes. Schones' lab is examining how external forces like diet and environment alter a person's chromatin — the all-important "packaging" that compresses our DNA inside each cell and also controls which parts are turned "on" or "off" properly. Some of those changes may persist even after the patient loses weight.

Within that investigation, Schones and his team are going where few have gone before: He's discovered that nearly half of the changes to chromatin take place at "transposable elements" (TEs), also known as "jumping genes" because these DNA sequences move from one part of the genome to another.

"Our work represents the first attempt to assess the consequences of TE dysregulation in obesity and how this contributes to long-term disease risk," he said.

Why City of Hope?

"It's so unlike a university setting," he said. "Being near patients has totally changed the way I think about my work. Now I think much more about how my research may one day solve clinical problems.

"And that's the cool thing about City of Hope. Even if our lab doesn't solve a specific problem, there are so many opportunities to share our research with others here who just may do it."

Passing the Torch

BY JEAN SUZUKI

City of Hope's diabetes research program has been shaped by visionaries such as Rachmiel Levine, M.D., who in 1949 discovered the action of insulin at the cell membrane, and the team of Arthur Riggs, Ph.D., the Samuel Rahbar Chair in Diabetes & Drug Discovery, and Keiichi Itakura, Ph.D., who in the 1970s were the first to create technology that led to the development of synthetic human insulin.

Their achievements inspired others, including two researchers who, early in their careers, made important discoveries that launched groundbreaking new areas of diabetes research: Yoko Fujita-Yamaguchi, Ph.D., professor emeritus of the Diabetes & Metabolism Research Institute at City of Hope, and Rama Natarajan, Ph.D., the National Business Products Industry Professor in Diabetes Research and chair of the Department of Diabetes Complications & Metabolism.

In 1980, Fujita-Yamaguchi was a young protein chemist who received her first National Institutes of Health grant as a principal investigator. Her research hoped to understand how insulin binding to its cell surface receptor stimulated molecular mechanisms within the cell.

Rama Natarajan, Ph.D. (left), with Yoko Fujita-Yamaguchi, Ph.D.

At that time, the insulin receptor's specific function at the cell surface remained a mystery, but Fujita-Yamaguchi was able to confirm what had eluded others before her — that insulin bound to its cell receptor stimulated the activity of a type of enzyme called tyrosine kinase inside of the cell.

> "To see the success of the next generation gives me the greatest pleasure."
>
> Rama Natarajan, Ph.D.

Fujita-Yamaguchi's discovery was a breakthrough in understanding how insulin functions in cells. Her work inspired new research that led to the identification of cell-signaling pathways, such as those that mediate the process of bringing glucose into a cell. Soon after, she successfully cloned the insulin growth factor-1 (IGF-1) receptor, which has been found to play a key role in cell survival and, importantly, cancer.

As a result of Fujita-Yamaguchi's contributions, interest in diabetes research continued to grow at City of Hope. In the 1980s, the Department of Diabetes, Endocrinology & Metabolism was established. Talented diabetes researchers were soon attracted to the program, including Natarajan, who joined City of Hope in 1990 and was pivotal in expanding the field of diabetes research into new and exciting areas.

In the early 1990s, Natarajan identified the role of inflammation in diabetes complications. She was able to link high glucose levels with increased vascular inflammation — a hallmark of diabetic complications such as kidney and heart disease.

This early work sparked her interest in epigenetics.

Epigenetics is the study of heritable changes in gene expression that occur without changes in the underlying DNA sequence of the gene. What can change is whether certain genes get switched on (expressed) or switched off (inhibited) as a result of external factors. In this way, external factors can alter epigenetics to influence the development of human diseases.

"With epigenetics, we ask the question, 'What about the environment and lifestyle, and how do they affect the onset and severity of diabetes and its complications?'" Natarajan explained.

Natarajan was the first to demonstrate the role of epigenetics in diabetic vascular inflammation and the first to characterize the epigenetic mechanisms involved in diabetic kidney disease. She was also one of the first to show the involvement of epigenetic mechanisms in the phenomenon of metabolic memory, in which periods of prior high blood sugar levels predispose patients with diabetes to long-term persistent complications, despite normalized blood sugar levels.

The connections she identified between epigenetics, inflammation, diabetic complications and metabolic memory have transformed the field. But she acknowledges that there is more work to be done.

"There are excellent drugs now to treat diabetes itself, but people still continue to suffer from complications," Natarajan said.

Her pioneering studies are driving the development of novel therapeutic approaches. Unlike genetics, epigenetics is reversible and yields opportunities for therapeutic intervention.

For Fujita-Yamaguchi and Natarajan, their legacy extends beyond the lab, as both are actively involved in mentoring the next generation of scientists — Fujita-Yamaguchi as the director of the City of Hope — Japan Scientific and Educational Exchange Program and Natarajan as chair of the Women's Leadership Committee.

"To see the success of the next generation gives me the greatest pleasure," Natarajan said.

Generation to Generation:

The Riggs Connection

BY ABE ROSENBERG

Hear more from Arthur Riggs, Ph.D.

From longtime administrators to veteran faculty to next-generation researchers, so many diabetes specialists smile and mention the same name when asked why they chose City of Hope. No surprise: Arthur D. Riggs, Ph.D.

Beloved, even revered at City of Hope for over four decades, Riggs, the Samuel Rahbar Chair in Diabetes & Drug Discovery and director of the Diabetes & Metabolism Research Institute at City of Hope, has made history while also making a profound impact on hundreds of scientists and clinicians.

"It is just awesome to work with the guy who [helped develop] synthetic insulin," gushed Jeannette Hacker-Stratton, a type 1 diabetic and administrative program manager for the Islet Cell Transplantation Program. It was Riggs' research in 1979 that paved the way for the bacterial production of synthetic human insulin, leading to the formation of Genentech and kickstarting the biotech industry.

Sampath Rangasamy, Ph.D., a researcher at City of Hope affiliate TGen, spent his early years in rural India struggling to control his own type 1 diabetes with animal-based insulin. Once he moved to a larger city and could access the fruits of Riggs' labor, Rangasamy's life changed dramatically. Years later, when he met Riggs for the first time, the encounter was … interesting.

"TGen and City of Hope had this gathering," he recalled, "and I got super excited to see [Riggs] there, and a little star-stuck about approaching him to introduce myself.

"But after I gave my presentation, it was Riggs who came over to me!" he exclaimed. "He said to me, 'Excellent job!'

"Now we talk frequently. He's a great person."

Fellow researchers at City of Hope tell of similar experiences. Riggs interacts with many of them frequently, not as some Olympian-on-high making pronouncements, but rather as mentor, colleague and friend, collaborating and suggesting.

"My philosophy for scientific leadership is to make suggestions, almost never orders," Riggs explained. "This is what my mentors did."

His role model at Caltech, Herschel K. Mitchell, Ph.D., "only made suggestions. It was OK for me to question his suggestions, and he encouraged me to make my own decisions. I was expected to think independently."

He found the same encouragement at the Salk Institute, where Melvin Cohn, Ph.D., guided him. Later, at City of Hope, it was biologist Susumu Ohno, Ph.D., who created an environment where "ideas and theoretical discussions again were an important part of our research effort at that time," said Riggs, "and this continues to this day."

Indeed it was an idea — and a suggestion from Riggs — that fundamentally refocused the work of one of City of Hope's prominent research teams.

> "My philosophy for scientific leadership is to make suggestions …"
>
> Arthur Riggs, Ph.D.

"Our lab direction changed five years ago," recalled researcher Dustin Schones, Ph.D. His team studies how obesity may bring about genetic changes that could lead to diabetes. A graduate student believed she'd detected changes in so-called "transposable elements" — DNA sequences that change location.

"We'd largely ignored TEs," said Schones. "But Dr. Riggs suggested to the student that she look further." She did, and now Schones' lab leads the way in this emerging area, examining the consequences of TE dysregulation.

Schones says this is exactly what he was looking for when he joined City of Hope following his postdoctoral work at the National Institutes of Health.

"Art Riggs is one of the reasons we moved to City of Hope."

A strong draw who doesn't come on strong. Not one to pull rank or stand on ceremony, Riggs makes a point of being accessible, just as his mentors did for him.

"I would like to think I am approachable," he said. "My office door is open … and I do try to be as nice as I can to everybody."

Investing in Hope

Chuck and Nancy Trudeau are eager to tell others about the advantages of using real estate to fund a charitable remainder trust to benefit City of Hope. "We retired from teaching nine years ago," said Chuck. "Nancy was an elementary school teacher, and I was a high school teacher and principal. We were looking for ways to make our lives simpler. Getting rid of our responsibilities as landlords for 40 years was part of it."

Coincidentally, a friend and fellow City of Hope supporter shared an article about gifting real estate to fund a charitable remainder trust (CRT). Intrigued, Chuck called his accountant and financial advisor. After researching the benefits, their advisors agreed with the Trudeaus that a CRT could address both their financial needs as well as their wish to support City of Hope.

"We wanted to do some good in the future while receiving a steady cash flow for the rest of our lives." The experience was so positive that they have donated a second property. Nancy added, "We looked at the numbers with our CPA and with the income from the CRT and the tax benefits, we're coming out ahead financially — and no more calls about a broken hot water heater in the middle of the night!"

The Trudeaus chose to designate their gift to a program that is very meaningful to them — pediatric cancer research. Cancer has touched both Nancy and Chuck's lives. Nancy's parents and grandparents each developed cancer at early ages ("Back then, you couldn't even say the word 'cancer' — we called it 'The Big C'"). Chuck's father and three grandparents died of cancer as well.

The Trudeaus believe that investing in City of Hope by establishing a CRT is the best way to help eradicate cancer. "Treatment has come a long way, but we're not there yet. We must find a cure and City of Hope is our best chance."

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

Double Jeopardy

Endocrinologist Raynald Samoa, M.D., specializes in treating cancer patients with diabetes

BY MALCOLM BEDELL

Raynald Samoa, M.D., endocrinologist and assistant clinical professor in the Department of Clinical Diabetes, Endocrinology & Metabolism at City of Hope, plays an unusual role in the treatment of some types of cancer: He specializes in treating patients with preexisting type 1 or type 2 diabetes, as well as patients who develop diabetes as a side effect of some types of cancer treatment.

INSIDE THE ENDOCRINE CLINIC

"In our endocrine clinic," Samoa said, "we treat patients on an outpatient basis, and we do a lot of things that are sort of the bread and butter of other endocrinologists: We manage diabetes, we manage thyroid conditions, we treat thyroid cancer and hormonal disorders. But we also see a lot of patients who need metabolic help."

Samoa sees patients who are at several different stages of cancer treatment, as well as patients at risk for type 2 diabetes who may be able to use lifestyle modification regimens to offset their chances of developing it, and potentially change the course of their cancer progression as well.

Children make up a significant portion of his practice. "Most of the pediatric patients I see fall into two categories," he said. "They are either cancer survivors with a hormonal problem such as adrenal insufficiency or hypothyroidism, or I am treating them for thyroid cancer."

As for adult patients, "We're starting to see patients at earlier stages of their [cancer] treatment who are showing early signs of metabolic derangement," he said. "We evaluate these patients in clinic to determine how their insulin resistance came about, we talk about the four pillars of treating insulin resistance (including eating healthier, getting more exercise, getting optimal sleep and managing stress) and we try to institute environmental and behavioral change. Here at City of Hope, we use these modifications specifically to see if they change the course of cancer."

INSULIN RESISTANCE AS A GATEWAY TO CANCER

"Unlike type 1 diabetes, where there's an absence of insulin, type 2 diabetes comes from metabolic changes that make it harder for people to use their insulin, and they become insulin resistant," Samoa said. After a prolonged period of poor nutrition, lack of exercise, high consumption of alcohol, poor stress management or other lifestyle issues, the body can no longer use insulin efficiently. "Even though they're making a lot of insulin, they're not making enough to overcome their resistance," Samoa said.

"This creates an environment in the body that's beneficial to cancer. One of the things insulin does is make things grow in the body. And high blood sugars are very effective in feeding cancer cells," Samoa explained. "So when your body is producing high amounts of insulin, and blood sugars are relatively high, that provides the optimal environment for cancer cells to flourish." Thus, while the type 2 diabetes treatment protocols are essentially the same for cancer and noncancer patients, "controlling blood sugar becomes even more important to the care of patients being treated for cancer."

Raynald Samoa, M.D.

Some cancer treatments can also increase patients' susceptibility to type 2 diabetes. "For example, steroids like prednisone are used in many chemotherapy regimens, and they significantly decrease one's ability to control blood sugars," Samoa said.

Many of the other side effects of cancer treatment, including loss of appetite or muscle loss due to reduced physical activity, can cause metabolic changes that can lead to type 2 diabetes. "This leads to a sort of 'perfect storm' for the disease," Samoa said.

IMMUNOTHERAPY AND TYPE 1 DIABETES

Some of the most effective forms of cancer treatment, including immunotherapies that use

the body's own immune system to help fight cancer cells, can also cause type 1 diabetes in patients with no prior history of the disease. Checkpoint inhibitors, for example, which help block proteins in the body that inhibit this immune system response, may also stop the pancreas from producing insulin. While this side effect is uncommon, it may lead to clues about how type 1 diabetes develops in noncancer patients.

The laboratory profile of type 1 diabetes caused by the use of checkpoint inhibitors is different than "regular" type 1 diabetes. According to Samoa, in a cancer patient with treatment-related type 1 diabetes, "we're seeing that the beta cells of the pancreas don't appear to be damaged — but we know they're not producing insulin. One of the theories is that the immune system may be blocking the pancreas from functioning.

"Checkpoint inhibitors target certain markers in the body, which allows us to narrow the field for which of those markers lead to diabetes," Samoa explained.

REDUCING TYPE 2 DIABETES RISK MAY ALSO REDUCE CANCER RISK

"Diabetes and cancer are tied together. Exploration of one leads to new discoveries about the other," Samoa explained. But research is only part of his work. Helping cancer patients untangle the path that led to their insulin resistance is a major part of Samoa's day-to-day life as a clinician.

"I run the MetFit program here at City of Hope, which is a lifestyle modification program that tries to help people reduce their insulin resistance to help prevent or manage chronic disease like high blood pressure, diabetes and liver disease."

Samoa's dedication to lifestyle modification extends beyond the walls of City of Hope. He's also organized a version of his program that takes place in the community, called "Roots of Hope." In a partnership with the Episcopal Diocese of Los Angeles, Samoa hopes to spread his message in the community before patients have to set foot in a hospital. "Part of the reason I'm so interested in lifestyle modification is its potential to prevent cancer," Samoa said.

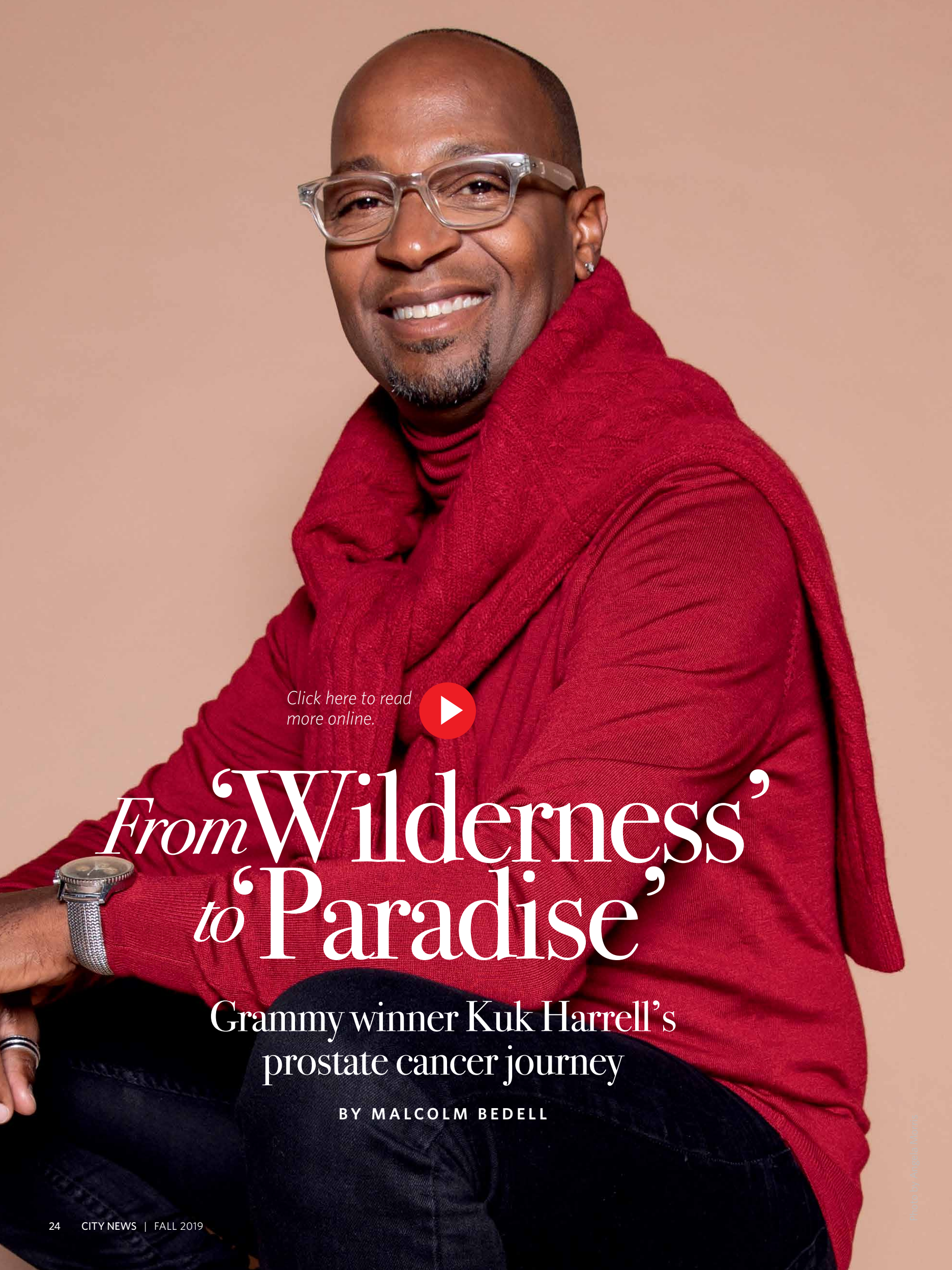
This kind of "whole body" approach to overall lifestyle modification as a means of helping to treat, better understand, or even prevent cancer and diabetes is unique to City of Hope. "There are no models for this kind of treatment to copy," Samoa said. "We're building it from the ground up. "

Pioneering Passion and Perseverance

Type 1 diabetes has had few rivals as fiercely dedicated to its cure as Thomas J. Beatson Jr., a longtime survivor who died in 2016 at the age of 83 after living with the disease for 73 years. His Arizona-based Thomas J. Beatson Jr. Foundation awards grants for innovative research and education aimed at a cure for type 1 diabetes, and City of Hope is a recent beneficiary. The Beatson Foundation has gifted a $500,000, two-year grant to support research into an oral compound for diabetes-related peripheral neuropathy led by Arthur D. Riggs, Ph.D., the Samuel Rahbar Chair in Diabetes & Drug Discovery, who runs the Diabetes & Metabolism Research Institute at City of Hope.

A pioneer in the creation of synthetic insulin in the 1960s, Riggs is just the scientist to forge new tools in the fight against peripheral neuropathy, the numbness and sensitivity in the extremities that results from nerve damage caused by high blood glucose levels. Diabetic neuropathy affects approximately two-thirds of diabetes sufferers and can lead to irreversible damage and even amputations. Blood glucose control through an oral compound could help slow its progression and bring about better outcomes.

A native of New Rochelle, New York, Beatson was diagnosed with type 1 diabetes at age 10. He became an engineer and moved to Phoenix to work in General Electric's computer systems department, retiring in 1987. Beatson supported cutting-edge diabetes research for much of his life through Harvard's Joslin Diabetes Center and other organizations, even participating in studies himself and funding a playroom for children with diabetes at Joslin. A determined leader in the fight against type 1 diabetes, Beatson refused to let the disease keep him from his passion for sport cycling, an activity he developed in his forties that ultimately involved biking more than 100,000 miles over 30 years with his insulin pump attached to his bike shorts. The new research grant allows Beatson's shining perseverance and hopeful spirit to continue.



Click here to read more online.

From ‘Wilderness’ *to* ‘Paradise’

Grammy winner Kuk Harrell’s prostate cancer journey

BY MALCOLM BEDELL

Photo by Angela Adams

When prostate cancer comes calling, it doesn't count how many Grammys you have sitting on your shelf. The most common cancer among American men after skin cancer, prostate cancer affects nearly 175,000 each year. Prostate cancer will impact about 1 in 9 men, and in 2018, it came calling for Kuk Harrell.

When it comes to the top talent working in pop and R&B vocal production and engineering today, few are more accomplished or more sought-after than Harrell. His work with Mary J. Blige, Beyonce and Rhianna has earned him five Grammys. He has joined forces with the biggest names in music today, including Celine Dion, Mariah Carey, Lionel Ritchie, Justin Bieber, Katy Perry and Britney Spears. He's given notes to Kanye, collaborated with Cher and shared studio time with Kendrick Lamar. But his battle with prostate cancer could be Harrell's biggest challenge to date.

In 2018, a prostate-specific antigen (PSA) test first revealed elevated levels that pointed to cancer. "When my physician first told me that my numbers were concerning, I was shocked and scared," said the 54-year-old Harrell. "During that first visit to the urologist, I was terrified. I just didn't want to hear the diagnosis." Because of Harrell's family history and the high rate of occurrence in African American men, doctors prepared Harrell for the worst: prostate cancer.

Harrell searched for ways to turn his fear into an opportunity to lead and inspire others. "The first person I told was my wife, followed by my manager," he said. "They were freaked out, but by the time I started telling people the news, I realized that with all of the things that God has done in my life, I'm supposed to beat this. I'm supposed to be a miracle." Harrell's confidence transformed him from victim to counselor, as he used his diagnosis to encourage and reassure those around him.

After having his prostate removed in Atlanta, Harrell's manager and an associate urged him to seek ongoing treatment at City of Hope, where the quality of care was immediately evident.

"My patient coordinator, Lupe Santana, met me at the front door, walked me through the facility and made the process very clear," Harrell said. He was treated by Tanya Dorff, M.D., associate clinical professor, Department of Medical Oncology & Therapeutics Research, and Savita Dandapani, M.D., Ph.D., assistant clinical professor, Department of Radiation Oncology.

Harrell's cancer was considered "locally advanced" because it had spread outside of the prostate itself but not outside of the pelvis, according to Dandapani. "Mr. Harrell was considered curable at diagnosis," explained Dorff, "but unfortunately, his first surgical treatment failed. We didn't see any signs of metastatic cancer, but his blood test revealed warning signs that there were still cancer cells remaining."

> "I'm supposed to be a miracle."
>
> Kuk Harrell

From their first meeting, Harrell placed all of his confidence in his care team. "Dr. Dorff really listened to me, and she allowed me to ask questions," Harrell said. "I was confident in the fact that everything was going to be done in that one building, everyone would be talking to each other, and she would be overseeing the whole thing. I knew that there would be no way that I would slip through the cracks."

Following several weeks of radiation treatment, Harrell received hormone replacement therapy injections to return his testosterone levels to normal. "On the medical oncology side," explained Dorff, "we approach hormone therapy with lots of attention to mitigating side effects, and support for the patient as a whole person."

For Harrell, the name of the hospital felt well-suited to the care he received there. "Throughout the process, I felt nothing but hope. I knew that I could access any of the care I needed, or any of my test results, at any time of the day, and be taken care of. It made me feel at peace the entire time."

While Harrell described his cancer journey as "a wilderness," he also explained that it could be "a paradise."

"My seven-week radiation treatment was the best season of my life....It gave me an opportunity not just to witness to others, but to see that life can hand you challenging moments, and still allow you to find peace. I want the staff at City of Hope, anyone that's touched this body, to know how amazing and incredible they are."

Today, Harrell's PSA tests show that he has "achieved an excellent remission," according to Dorff, with cancer indicator levels that are "undetectable." He will be checked again in six months after his testosterone levels return to normal to ensure the hormonal recovery doesn't correlate with a rise in PSA levels. At this point, Harrell's doctors are "very encouraged" by his progress.

"I'm still here, and I'm not checking out," Harrell said. "Let's ride this thing until the wheels fall off."

Each November, City of Hope hosts a NoShaver fundraising and awareness campaign to inspire conversation, encourage testing and raise critical funds for prostate cancer research conducted at City of Hope. To find out more, go to ***OurHope.CityofHope.org.NoShaver.***

Motivated by a Message of Giving

According to Paul Lester, his sister, Monica Lester, was most passionate about communication — how to motivate others, in particular. With its recent philanthropic gift to support diabetes research at City of Hope, the Monica Lester Charitable Trust hopes to motivate top-notch scientists to discover new and better ways to combat the disease.

It is a very personal mission for the Lesters. Both Paul and Monica, who was three years older than her brother, were diagnosed at a very young age. "We've been in touch with it our whole lives," said Paul. "We were always interested in trying to help other people with diabetes, particularly children." The L.A.-based trust created in Monica's honor has given grants to encourage medical research at places such as Cedars-Sinai Medical Center, the Prostate Cancer Foundation and Children's Hospital, and trustee Frank Lee recently recommended supporting City of Hope's efforts, as well. "Of course, both my sister and I had known for years that City of Hope would be a good venue to invest in," said Paul, who is also a trustee along with Joel Levine. "So it seemed like a wise thing to do."

Born in 1947, Monica graduated from UCLA with a psychology degree and went on to acquire her doctorate in philosophy from the University of Vienna. She worked in corporate communications and taught speech and rhetoric at private institutes in Europe before passing away in 2014 from complications driven by her diabetes. "It's a good thing to help people struggling with something you've lived through yourself," said Paul. "And hopefully at some point we can help them avoid it altogether."

Throughout her life, Monica made it her calling to understand "how best to talk to people, how to impart messages," Paul said. With this gift, the Lesters have sent a message of aspiration and optimism to all who grapple with diabetes.

Best in the West

U.S. News & World Report names City of Hope tops in the West in its 2019-20 Best Hospitals: Specialty Rankings

City of Hope is the leading cancer hospital in the West, according to U.S. News & World Report's 2019-20 Best Hospitals: Specialty Rankings issue. This marks the 13th consecutive year that it has been distinguished as one of the nation's elite cancer hospitals.

Click here to read more online.

"City of Hope is extremely honored to be recognized by U.S. News & World Report for our long-standing commitment to providing the best treatment and care to our patients," said Robert Stone, City of Hope president and CEO. "It's a reflection of our exceptional, compassionate care and our dedication to turning powerful science into lifesaving new treatments for our patients.

"A steadfast collaboration between City of Hope scientists and physicians, our strong translational research model and our top-notch biomedical research and manufacturing facilities enable us to deliver excellent cancer care," Stone added.

RANKED NO. 4 IN PATIENT EXPERIENCE

This year, U.S. News & World Report added data from Hospital Consumer Assessment of Healthcare Providers and Systems, which tracks exemplary patient experience. City of Hope was ranked fourth in the country out of 885 hospitals surveyed.

City of Hope was also ranked "high-performing" in lung cancer surgery and colon cancer surgery.

"Although City of Hope is not driven by the accolades we receive, we know that patients and their families often turn to rankings and ratings to decide where to get their care," said Michael Caligiuri, M.D., president of City of Hope National Medical Center and the Deana and Steve Campbell Physician-in-Chief Distinguished Chair. "We are gratified to be recognized as a leading-edge cancer center where a patient's hope can turn into reality through our innovative treatments and exemplary care."

The cancer hospital ranking is compiled based on data from 885 eligible cancer hospitals nationwide; U.S. News & World Report's rankings cover 16 specialty areas in total. Only 12.5% of the more than 4,500 hospitals analyzed in all the specialty areas received the "Best" status. A cancer hospital's overall score reflects performance in such areas as advanced technologies, designation as a National Cancer Institute comprehensive cancer center and survival score data.

> "It's a reflection of our exceptional, compassionate care."
>
> Robert Stone,
> City of Hope president and CEO

1 OF JUST 50 COMPREHENSIVE CANCER CENTERS

City of Hope is one of 50 comprehensive cancer centers in the nation, the highest designation possible from the National Cancer Institute and a metric used by U.S. News & World Report. To earn this designation, a center must undergo a rigorous peer-review process, maintain a high number of cancer research projects and be heavily involved in community outreach, as well as meet other academic and public service requirements. City of Hope earned its comprehensive cancer center designation in 1998 and has maintained it since.

City of Hope is also a founding member of the National Comprehensive Cancer Network, making it a leader in advancing research and treatment protocols throughout the nation. City of Hope is currently conducting 500 clinical trials, enrolling more than 6,200 patients.

HIGHEST LEVEL OF ACCREDITATION

The American College of Surgeons Commission on Cancer recently awarded City of Hope a "Three-Year With Commendation" designation, its highest level of accreditation recognizing exceptional cancer care.

City of Hope was a pioneer in bone marrow and stem cell transplants, and continues to have one of the largest, most successful such programs of its kind in the U.S. The Center for International Blood and Marrow Transplant Research Center has ranked City of Hope as an "overperforming" transplant center, making it the only U.S. transplant center with this recognition for 14 consecutive years. Interlink COE Networks and Programs also recently designated City of Hope's bone marrow and stem cell transplant program as No. 1 in the nation.

A leader in the CAR T field for being the first to offer CAR T trials for specific targets on glioblastoma and acute myeloid leukemia cells, City of Hope has treated more than 350 patients in CAR T trials and currently has 20 ongoing CAR T cell and T cell trials.

City of Hope is ranked the leading cancer hospital in California by U.S. News & World Report and, most important, by Ivan Garcia-Burgos, cancer survivor.

We are honored to have the highest U.S. News ranking in the state, yet it's our patients' health and well-being that provides us with the only validation we need.

Remission, our only rest point.

A full cure, the only goal.

Our patients are at the forefront of everything we do and every decision we make.

That's why we're committed to delivering the best clinical care possible, from relentless research and innovative treatment to unparalleled compassion for every City of Hope patient.

At City of Hope, we'll continue to put cancer patients and their families first.

That won't stop until we stop cancer.

Discover more at **CityofHope.org.**

BEST HOSPITALS U.S.News & WORLD REPORT NATIONAL CANCER 2019-20

City of Hope®

Lifetime Crusade

For this diabetes researcher, the mission hits close to home

Growing up on a farm in rural India, Sampath Rangasamy, Ph.D., practiced every morning for his beloved cricket matches.

Then, in middle school, he dropped 10 pounds from his lanky frame within a week. Insatiably hungry and thirsty, he started urinating frequently.

Two weeks later, he slipped into a coma. His father rushed him to the hospital on the back of his motorcycle.

"The diagnosis of type 1 diabetes was very devastating for my family," explained Rangasamy, now a research assistant professor at TGen, an affiliate of City of Hope. "In Asians, type 1 is a rare disease, compared to Caucasians, and there is even a little taboo around it. In my community, the doctors had never seen it."

Sampath Rangasamy, Ph.D.

A LIFETIME CRUSADE

The young Rangasamy set out on a lifetime crusade against the disease that would define his career but not his character: He sent letters to the British Diabetes Association (BDA) to request educational pamphlets in the mail. He made "pen friends" with patients in Europe, whom he found through the BDA magazine. Though his family did not want to share the news of his diagnosis due to stigma, Rangasamy wanted to learn as much as he could.

"My doctor had trained in the U.S. and wanted to serve in a rural community — and that was the biggest thing for me because he not only treated me, he also educated me and, in turn, I tried to educate him, and my school friends and my school teachers," Rangasamy explained. "In two years, I thought I was an expert in type 1 diabetes."

In the 1980s, in rural India, Rangasamy self-administered up to four animal insulin shots daily in his legs, using a glass syringe with a steel needle that he sterilized every time. The family did not have a glucose meter, so his mother boiled Benedict's solution with his urine to determine his glucose levels by sight. Rangasamy had an allergic reaction to the animal insulin, which caused lipoatrophy, or a localized loss of fat tissue, that left behind scars he carries to this day.

THE MAN BEHIND HIS MOTIVATION

"When I finished high school, I went to a big town in India to talk to a specialist in diabetes, and I learned that there were disposable syringes and testing strips and recombinant human insulin," he said. "After that, I started taking recombinant insulin. It gave me more control. This motivated me to research diabetes."

Last year, Rangasamy met the man behind his motivation, Arthur Riggs, Ph.D., the Samuel Rahbar Chair in Diabetes & Drug Discovery and director of the Diabetes & Metabolism Research Institute at City of Hope. Riggs is renowned for his work on synthesizing the first man-made gene and using synthetic genes to produce human insulin, work that transformed Rangasamy's life more than 30 years ago and sparked his career in diabetes research.

In September 2018, the National Institutes of Health awarded a $2.8 million grant to a consortium led by TGen and University of New Mexico in a groundbreaking effort to discover new treatments for diabetic retinopathy, one of the primary complications of both type 1 and type 2 diabetes, and one of the leading causes of blindness in America, affecting as many as 24,000 patients each year. Rangasamy is the study's principal investigator at TGen.

"Diabetic retinopathy, with loss of vision, is a serious, common and debilitating problem associated with the complications of diabetes," Riggs said. "This study is an exciting approach to understanding the molecular and genetic mechanisms involved, and it makes use of the extraordinary technology and expertise available at TGen and City of Hope."

The study will use genomic sequencing to identify genes associated with the condition and establish a molecular profile that can predict the severity and treatment of the disease for each patient.

HOPE FOR THE FUTURE

As a teen, Rangasamy was discouraged from playing cricket due to stigma associated with type 1 diabetes. As a young man, his parents feared he might not be able to marry if he disclosed his condition. Though the taboos of his home country have faded, he still battles very real effects from the disease.

"Even with an insulin pump and a continuous glucose monitor, I have to put in an extra two hours each day to take care of myself," he said. But Rangasamy is also hopeful to see how his work can contribute to the legacy of leadership in diabetes research at City of Hope.

In 2017, City of Hope announced The Wanek Family Project for Type 1 Diabetes. This ambitious project seeks to reawaken insulin-producing cells and to harness immunotherapies to find a cure for the disease.

"After living with type 1 for a long time, it is very important for me to have a cure," Rangasamy said. "Even though I am a scientist and I know it may take a long time, I am dreaming for a day when I can have a cure and have a normal life."

A Multigenerational Legacy of Investments in Humanity

From left to right: Fouad Kandeel, M.D., Ph.D.; Louis Gonda, Lorena Gonda; Arthur D. Riggs, Ph.D.; William Davis; Elizabeth LaBorde

In May, Louis and Lorena Gonda visited the City of Hope campus to view the installation of a new, crucial piece of equipment — a Milo system with scanner for measuring protein expression at the single-cell level — in the facility named after their parents: the Leslie & Susan Gonda (Goldschmied) Diabetes & Genetic Research Center. It was just the latest in a series of gifts the Leslie and Susan Gonda (Goldschmied) Foundation has made to enshrine and extend a multigenerational legacy that spans more than 20 years of support for City of Hope.

"We were very happy to see our gift installed, and we are optimistic that this next-generation biomedical research device will advance the work currently being done in the diabetes laboratories," said Louis and Lorena. (Their sister, Lucy, could not attend the installation.)

Launched in 1988, the Gonda Foundation was created with the purpose of advancing the treatment of diabetes and vascular disease, as well as supporting programs that further medical research and education around the world. The foundation has endowed facilities devoted to diabetes research in Israel as well as at UCLA, the Mayo Clinic and City of Hope, where the Gonda Center, completed in 1997, houses the Diabetes & Metabolism Research Institute at City of Hope run by Arthur D. Riggs, Ph.D., the Samuel Rahbar Chair in Diabetes & Drug Discovery. Riggs, who pioneered the creation of insulin via synthetic genes in the 1960s, established the Distinguished Chair in Diabetes & Metabolism Research held by Fouad Kandeel, M.D., Ph.D., an endocrinologist and expert in type 1 diabetes with a focus on islet transplantation. Kandeel made the request for the Milo system.

The Gondas' relationship with longtime City of Hope donor Arthur Kaplan led them to parlay their interest in supporting diabetes research and fund the Diabetes & Genetic Research Center building, an expansion of an initial building funded by the Gondas, as well as the most recent gift of the Milo system for Kandeel and the Diabetes & Metabolism Research Institute. Professor and chair of the Department of Clinical Diabetes, Endocrinology & Metabolism, Kandeel is exploring both the efficacy of islet cell transplantation to treat patients with type 1 diabetes and the genetic development of type 2 diabetes in the Hispanic population. The Gonda Foundation's funding was pivotal in creating the Southern California Islet Cell Resources Center (SC-ICR) co-directed by Kandeel. The SC-ICR supports new developments in the prevention and treatment of diabetes, including the Islet Cell Transplant Program that Kandeel oversees.

"Diabetes has greatly affected our family," said Louis and Lorena. "We have always been impressed with the great work City of Hope is doing in this area under the direction of Dr. Kandeel and his team."

Leslie and Susan Gonda survived World War II-era depredations in Eastern Europe before marrying and emigrating to the United States in 1963. Ten years later, Leslie and Louis created what became one of the most successful airplane-leasing companies in the world, International Lease Finance Corporation. To honor their good fortune, Leslie and Susan insisted on making "investments in humanity" that would allow them "to share the American dream with others around the world." Their children carry on that mission today with the help of Foundation Management president Cheryl Zoller, who has managed the Gonda Foundation for 30 years (Susan passed away in 2009, Leslie in 2018). Together, they hope to continue to cultivate a partnership that through City of Hope has benefited so many patients in their struggle with diabetes.

"The Gonda family's recent gift in honor of our parents continues the intention of Leslie and Susan Gonda to support progress in diabetes for many generations to come," said Louis and Lorena.

Everything You've Heard About Type 1 Diabetes Is Wrong

BY WAYNE LEWIS

Type 1 diabetes has long been thought of as an error of the immune system in which the body's defenses misidentify insulin-producing beta cells — found in structures of the pancreas called "islets" — as foreign or defective. But a landmark 2017 study led by Bart Roep, Ph.D., holder of City of Hope's Chan Soon-Shiong Shapiro Distinguished Chair in Diabetes, has turned that idea on its head.

City News sought to debunk some of the misconceptions about the disease in a conversation with Roep, who also serves as director of The Wanek Family Project for Type 1 Diabetes and as professor and founding chair of the Department of Diabetes Immunology.

How did your 2017 findings change how you thought about type 1 diabetes?

I used to say that diabetes is a mistake of the immune system, and now I'm actually saying, "Instead, it seems to be a mistake of the beta cells."

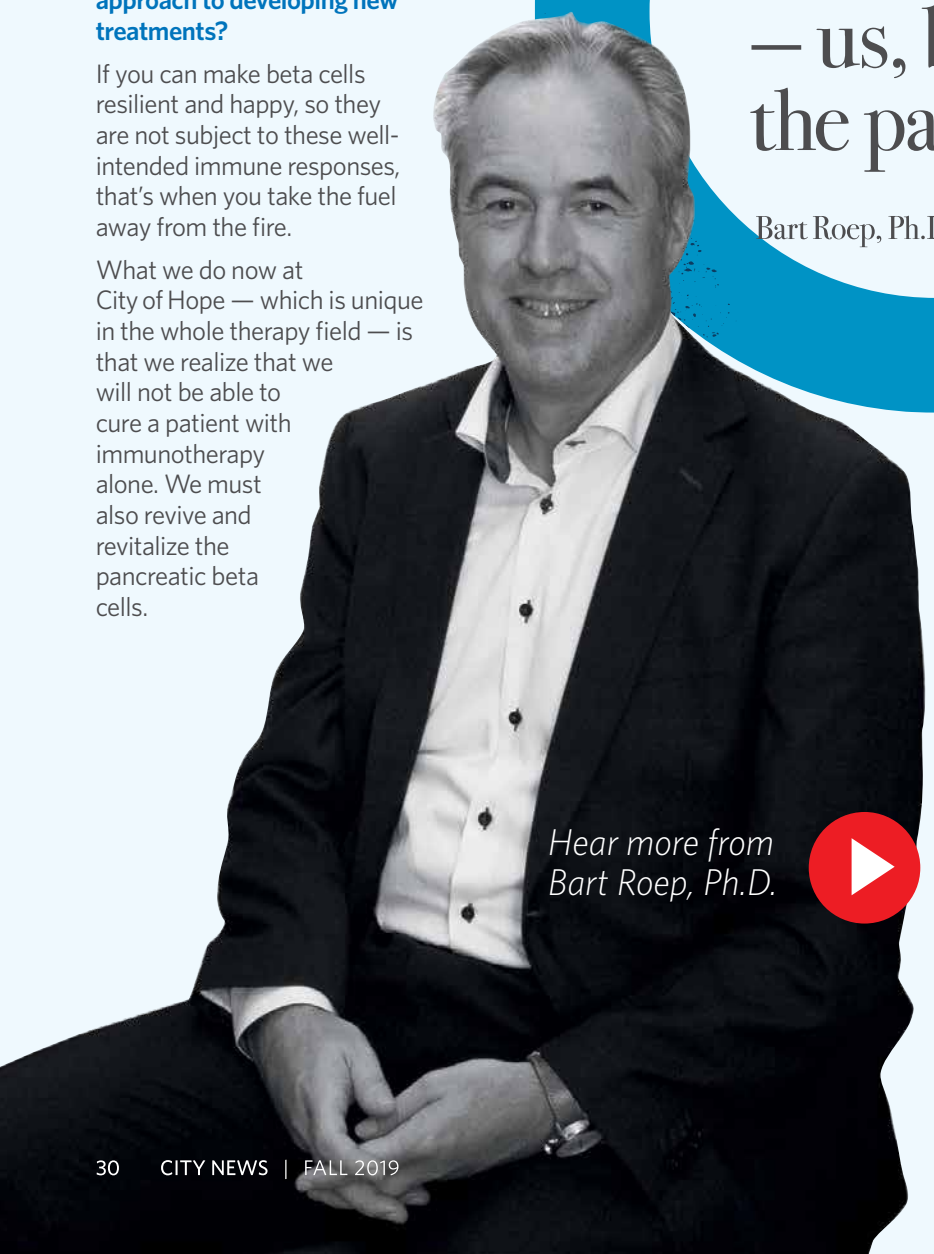
There are these changes that are incurred by stress, and the immune system tries to clean up. They're the same changes that you also see in cancers. So it's actually with good intentions that the immune system starts to respond to the distressed islets.

How does that influence your approach to developing new treatments?

If you can make beta cells resilient and happy, so they are not subject to these well-intended immune responses, that's when you take the fuel away from the fire.

What we do now at City of Hope — which is unique in the whole therapy field — is that we realize that we will not be able to cure a patient with immunotherapy alone. We must also revive and revitalize the pancreatic beta cells.

> "This is an exciting time for everybody — us, but also the patients."
>
> Bart Roep, Ph.D.



How else has the understanding of type 1 diabetes changed in recent years?

Not so long ago when I was doing post-academic training of physicians, I had a slide titled, "Everything That I Learned in Medical School About Type 1 Diabetes Is Wrong."

It starts with the genetics. Type 1 diabetes is not an inherited disease. At best, you can inherit an increased genetic risk for the disease. Basically, the risk genes for diabetes are the winners of the Middle Ages. They are the survivors of the plagues and epidemics. And they actually endow the carriers of those genes with the best immune system, one that cancer patients would wish to have.

Another one is, we thought that it's a children's disease. That turns out to be wrong. We used to think 80% of patients get diabetes before the age of 18, and now we think it's less than 50%. That means that most of type 1 diabetes occurs in adults. And that makes it more difficult to distinguish from type 2 diabetes, which used to be called "adult-onset diabetes."

And then, we thought it was antibodies at the root of the disease. It's not. It's the T cells in the immune system that are responsible for the destruction. But they're also responsible for regulating the immune response, so these T cells give you ways to potentially cure the disease.

What you'll see in textbook medicine is that the diagnosis is the end game in type 1 diabetes, since virtually all the islets have been destroyed and there's no insulin. That's not true. At "best," 50% is gone. So now we try to preserve those beta cells and get them back in action.

And finally, the most important one people say is that type 1 diabetes cannot be cured. But yes, it can be cured. Even if it is only a few patients so far, the proof is there, even from my own work, that you can cure people with type 1 diabetes.

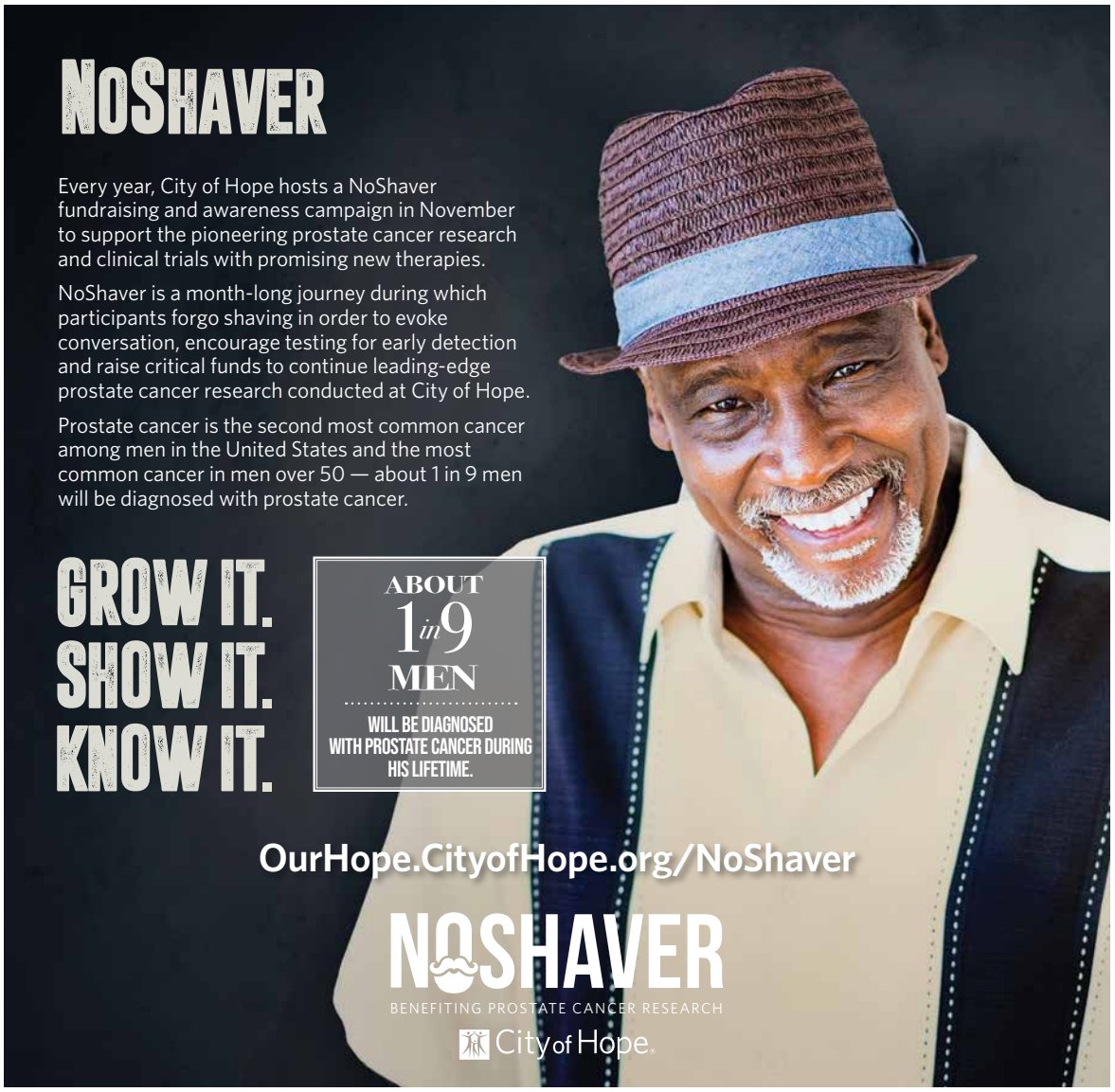
What do we mean when we say "cure"?

With the different forms the disease takes, there will not be a magic bullet. There will not be a single therapy that can treat everybody in the same way.

A few years ago, we raised eyebrows. Some were unhappy with our claim that we want to cure type 1 diabetes in six years. These days, when people ask, "Is it true that you want to cure diabetes in six years?" I say, "Well no, that's a misunderstanding. I want to cure diabetes today."

It reflects our sense of urgency. We cannot wait. It has taken too long since the discovery of insulin, and now we enter a new chapter where we go from dealing with the symptoms, coping with high blood sugar, to actually starting to treat the cause. This is an exciting time for everybody — us, but also the patients.

For some, stopping disease progression, halting the immune attack on beta cells and preserving some insulin production is a cure. For others, it is preventing diabetic complications that patients fear most. The goal of no longer injecting insulin is something that we ultimately strive for, but that's a very high bar. I fear that we will only be able to achieve that in a small number of patients, but it can be done. That we have shown. So let's not give up. Let's keep our hope, which is of course the keyword of our institute.



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City of Hope

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