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# Advancements For Life.

2020 Research Report

Children's  
Hospital  
LOS ANGELES

 American  
Diabetes  
Association®  
Research Foundation



# Introduction

## **To those dedicated to curing and preventing diabetes:**

Since the 1950s, the American Diabetes Association has been committed to providing critical funding to support innovative scientific discovery that translates to better treatment, healthier lives, and eventual cures. Despite the extraordinary challenges our nation and world faced this past year, the ADA has continued our commitment to our mission. This report outlines a few of the remarkable achievements made possible by your generous support.

In early 2020, the ADA responded quickly to the COVID-19 pandemic by pivoting to a targeted research strategy that allowed us to fund critical new grants, including the rapidly deployed funding of 10 research projects focused on the impact of diabetes on COVID-19, as well as the impact of COVID-19 on diabetes and its complications. The scientists awarded funding will allow us to better understand the biological mechanism underlying this risk, why some people are developing diabetes from COVID infection, and what we can do about it.

This pragmatic pivot taught us to look for opportunities to mobilize quickly to current crisis' with strong leadership, keen dedication, and an unwavering commitment to fiscal responsibility with our diverse group of funders.

ADA remains dedicated to supporting all of the key aspects of supporting research that have been part of our commitment for decades: support for early career investigators, to foster the next generation of leaders; support for investigator-initiated research through a core basic and clinical science research program, to generate the discoveries that will bring us effective new treatments and paths to a cure; and support for targeted research to accelerate those discoveries as unique opportunities arise.

While there are several lessons learned in 2020, the need for the ADA and our commitment towards research has never been stronger or clearer. Our programs, volunteers, and the support from all of you enable us to push forward along new frontiers in diabetes to prevent, cure, and improve the lives of all people affected by diabetes.

As we approach the 100th anniversary of the discovery of insulin, we can look back on a century of tremendous discovery that has transformed the lives of people with diabetes. Our job is not done, however, until we can eliminate the complications of diabetes and until we can prevent and cure diabetes.

We know you share our commitment to improving the lives of people with diabetes through a dedication to research. With your assistance, we can continue funding critical diabetes research and together we can conquer diabetes!

Our sincerest thanks,



**Robert Gabbay, MD, PhD**  
Chief Scientific and  
Medical Officer



**Robert H. Eckel, MD**  
President Medicine & Science



**Mary De Groot, PhD**  
President Health Care &  
Education

# Body and Soul

**When church members educate their congregation about diabetes, gains can be great**

## Meizi He MD, PhD, MSc

By Andrew Curry

There's lots of research on the effectiveness of using a church—as opposed to, say, a hospital—to teach people with diabetes the skills they need to manage their condition. Typically, professional diabetes educators offer classes in diabetes self-management to church members who find their regular place of worship a familiar and comfortable setting. Researcher Meizi He, MD, PhD, MSc, of The University of Texas at San Antonio calls this, “faith-placed” education. The approach has been widely tested in African American churches, where some studies suggest it improves adherence better than diabetes self-management classes held at hospitals or doctors’ offices.

Dr. He works in San Antonio, where diabetes is a particularly challenging problem among the city’s majority-Latino population. “The [Latino] community is disproportionately affected by the disease,” says Dr. He. Nearly 15 percent of Latinos in the United States have diabetes, 50 percent higher than the general U.S. population. “Particularly in low-income areas, they have limited access to health care, there’s a language barrier, and there’s limited access to healthy food.”

There was another statistic that spiked Dr. He’s interest: Over 90 percent of Latinos in the United States are affiliated with a church. That, she reasoned, would make churches great places to deliver health education. “We were looking for platforms to reach the target audience,” she says.

Dr. He wondered if classes incorporating Christian themes, taught by church members, might deliver more lasting results than faith-placed education. “We wanted to test the hypothesis that integration of faith is more effective than outside people coming to the church,” she says.

With the help of a grant from the American Diabetes Association (ADA), Dr. He designed an intervention called, “Building a Healthy Temple,” based on the well-known biblical verse from 1 Corinthians: “Do you not know that your bodies are temples of the Holy Spirit?”

After creating the intervention, Dr. He approached churches and recruited church members, typically the congregations’ lay members who had diabetes, to act as instructors. They were given a 40-hour training course and returned to their churches to deliver the same diabetes self-management support curriculum taught by professional diabetes educators, along with a sermon on health and seven sessions of health-oriented Bible study. “We try to connect diabetes to faith and scripture,” says Dr. He. “The message is people should maintain the temple, not for themselves, but because it’s God’s temple—and you’d better take care of God’s temple.”

To see if her curriculum was more effective, Dr. He had to find a way to compare church-based health education classes given by diabetes educators with “Healthy Temple” classes given by church members. To do so, she found



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Nutrition and Health Researcher at The University of Texas at San Antonio

**FOCUS**

Population Health

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**RESEARCH FUNDING**

Innovative Clinical Research

similar churches and paired them up, offering a Healthy Temple class in a large Catholic church and a regular diabetes education class in another Catholic church across town, for example.

The analysis compared the A1Cs of people who participated in classes run by members of their church to the A1Cs of those who took classes delivered by certified diabetes educators. Her initial results were encouraging: **The groups run by church members managed to lower their A1Cs significantly by the year mark**, and they kept their blood sugar (blood glucose) levels close to or within target range for a full year after the classes ended. The same benefit wasn't seen in the other groups.

The Bible-oriented classes were enthusiastically received. "People didn't see it as health education. They saw it as part of their faith practice," says Dr. He. "You can see the faith-based participants really liked it. People feel they're doing it for a higher purpose."

There's another factor at work, too. Even after the classes are over, participants stay in contact with other members of the group and their lay instructors, who are all fellow members of the congregation. "There's integration and ongoing support," says Dr. He. "People feel comfortable going to church and supporting each other."

And, says Dr. He, the community-based setting makes it easier to spread the message about diabetes

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**“PEOPLE DIDN'T SEE IT AS HEALTH EDUCATION. THEY SAW IT AS PART OF THEIR FAITH PRACTICE.”**

—MEIZI HE, MD, PHD, MSc

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management to the families and friends of those with diabetes. "Daughters and sons come to the classes to learn to support their parents," she says. "It's the beauty of a community-based program."

Combining faith and health wasn't without complications. One question Dr. He, herself a devout Christian, had to navigate was finding a way to connect caring for diabetes to respecting God, particularly for people who developed type 2 diabetes later in life. She was concerned, for example, that people with type 2 might see their diabetes as divine punishment for not caring for God's temple. "The program frames it in a positive way," she says. "You can honor God and move forward."

So far, Dr. He's results are in the research stage; she presented them at a recent ADA conference and is applying for funding to turn her research into a curriculum that could be adopted by churches nationwide and accredited by the ADA.

# Your Brain on Sweeteners

## Can low-calorie sweeteners contribute to diabetes?

# M. Yanina Pepino PhD

By Andrew Curry

In an effort to cut sugar without cutting sweet taste, people with diabetes often become heavy consumers of artificial sweeteners. Products such as aspartame, saccharin, and sucralose are part of a \$3 billion industry, used to flavor a wide variety of products by replacing sugar in everything from diet sodas to cookies and yogurt.

For most people, drinking sugar-free soda or eating an artificially sweetened cookie is based on a straightforward assumption that sugar substitutes don't do anything but add flavor—they're "free". As far as the body is concerned, in other words, liquid containing a no-calorie sweetener should be the same as water, but better (or at least sweeter) tasting.

But what if low- and no-calorie sweeteners play a role in promoting diabetes? In a long-term study of more than 750 people over age 65, heavy consumption of low-calorie sweeteners—the equivalent of three or more diet sodas a day—was associated with weight gain and higher rates of type 2 diabetes and heart disease.

University of Illinois Sensory Nutritionist, M. Yanina Pepino, PhD, is investigating what might be going on with the help of a grant from the American Diabetes Association. An expert on taste and metabolism who's spent more than a decade exploring the science of artificial sweeteners, Pepino admits the science is new—and confusing. "There's a lot of paradoxical data," she says.

For example, perhaps people who are overweight and therefore at a higher-than-average risk of developing type 2 diabetes, are more likely to be consuming artificial sweeteners in an effort to reduce their calorie intake. That doesn't necessarily mean diet soda caused their diabetes.

Pepino's research suggests there might be something else at play. Sweet taste, not sugar itself, may tamp down the body's response to insulin. When this happens, the cells don't take up glucose from the blood like they should, a condition known as insulin resistance. It's a known contributor to type 2 diabetes, along with the higher insulin production that usually follows.

To test her theory, Pepino gave 17 obese people a calorie-free drink containing sucralose, a common sweetener sold under the Splenda brand name that is 600 times sweeter than sugar (the drink was formulated to be a little sweeter than the typical diet soda). Afterward, she monitored how their bodies reacted to an oral glucose tolerance test, a common measure of how well the body handles glucose.

Pepino then repeated the whole procedure, but this time she gave the subjects plain water to drink before the glucose test. "If the artificial sweetener is really inert, then the [body's glucose response] should be the same as if you drink water," she says. "But we found it was not the same." Instead, the glucose tolerance test showed that the participants in the study were more insulin resistant after the sucralose drink than after water.



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 Innovative Research

“PEOPLE SHOULD CONSUME SWEETNESS IN MODERATION.

IT SHOULD BE A TREAT, NOT A DAILY, CONSTANT OCCURRENCE.

—M. YANINA PEPINO, PHD

Her early data also suggests that **there may be sweet taste receptors in the intestine that affect blood sugar (blood glucose)**. In a recent experiment, she asked participants to spit the sucralose drink out to see if just having the sweet taste would be enough to trigger a different response to the glucose test. This time, participants’ insulin levels didn’t rise as high as when the drink was swallowed, indicating less insulin resistance. This suggests the intriguing possibility that sweet taste signaling in the gut and the mouth independently regulate blood sugar.

In her latest experiment, Pepino is investigating hard-core artificial sweetener users to see if their reactions are different from those who don’t consume sugar substitutes regularly. In her earlier experiments, she tested the reactions of people who didn’t use artificial sweeteners regularly. This time, 20 volunteers who regularly consume artificial sweeteners and 20 who don’t will repeat the study to see if regular use changes the body’s response to the sweet taste and reduces the insulin resistance. “Perhaps if you use artificial sweeteners a lot, the brain doesn’t use sweetness signaling effectively,” she says.

It’s all part of an ongoing effort to figure out how these common food additives are affecting the body. Pepino is careful to stress that she doesn’t know for sure what’s going on, or whether all sugar substitutes cause the same responses as sucralose. But she is convinced that modern life is way too sweet. Readily available sweet flavors are a new phenomenon in the human experience: For our not-so-distant ancestors, sweetness would have been a rare treat, gleaned from ripe fruit or the very occasional raid on a beehive.

That suggests the importance of recalculating our relationship not just with sugar, but with sweet tastes altogether. “People should consume sweetness in moderation,” says Pepino. “It should be a treat, not a daily, constant occurrence.”

# Lack of Warning

## What's happening in the brain during hypoglycemia unawareness?

# Janice Hwang MD, MHS

By Andrew Curry

One of the most unpleasant, fearsome consequences of diabetes is hypoglycemia. It's what happens when your blood sugar (blood glucose) drops dangerously low. Symptoms usually include dizziness, shakiness, sweating, and intense feelings of hunger. "It's scary, and it feels terrible," says Yale School of Medicine endocrinologist Janice Hwang, MD, MHS.

As frightening as the symptoms of hypoglycemia can be, they are, in fact, a defense mechanism. They're the body's way of calling for help, prompting an immediate reaction: Get food, fast.

Yet after frequent hypoglycemic episodes, some people—particularly those with type 1 diabetes—develop what doctors call hypoglycemia unawareness. That's when blood sugar levels drop, but there are no symptoms to provide a warning. "That could put you in harm's way because the body's lost its defense mechanisms to tell you to act," Hwang says.

She wanted to know more about the causes of hypoglycemia unawareness—specifically, if the brains of people with hypoglycemia unawareness reacted differently to low blood sugar than those of people still sensitive to the body's signals. Ultimately, her goal was to see if hypoglycemia unawareness could be reversed so people could regain their warning systems.

With the help of a grant from the American Diabetes Association, Hwang set up an experiment using functional

magnetic resonance imaging and spectroscopy (fMRI/MRS), which monitors brain activity in real time. She put people with type 1 diabetes and a history of hypoglycemia unawareness on an IV drip of insulin and dextrose, a sugar the body converts into glucose. By adjusting the levels of sugar they were getting through the IV, she was able to artificially induce mild hypoglycemia and see what happened in their brains when their blood sugar got low.

When she compared their brain scans to scans of healthy individuals and to those of people with type 1 diabetes still sensitive to lows, the differences were obvious. "Frequent hypoglycemia and variable blood sugar can influence how blood glucose gets into the brain and is sensed," Hwang says.

In hypoglycemia-sensitive brains, regions connected to cravings and the brain's planning and control centers lit up in response to a drop in blood sugar levels. That makes sense: The priorities in a blood sugar crisis should be needing carbohydrate and figuring out how to get it.

In people with hypoglycemia unawareness, on the other hand, "Virtually no places in the brain light up," Hwang says. "When we expose them to moderate lows, people with hypoglycemia unawareness have very minimal changes in the brain."

Hypoglycemia unawareness is a short-term problem that often comes with long-term consequences. With no way to know when blood sugar is dipping dangerously low, hypoglycemia-unaware people can be reluctant to keep





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**RESEARCH FUNDING**

Clinical Translational Research

their blood sugar levels tightly managed. With higher blood sugar levels, they run a greater risk of complications such as retinopathy and cardiovascular disease later. Study after study has shown that tight glucose management is the best way to prevent long-term complications of diabetes. “If we could restore hypoglycemia awareness, it would go a long way to improving adherence,” says Hwang. “A big limiting factor to tight control is fear of hypoglycemia.”

What’s still unclear is whether hypoglycemia unawareness is reversible. Hwang hopes that knowing more about how hypoglycemia unawareness works will help researchers develop ways to turn it around.

Her next step is to set up experiments to investigate the current theory that sustained periods without hypoglycemic episodes can reboot the brain’s hypoglycemia sensors. To do so, her team has started a clinical trial to put patients with hypoglycemia unawareness on new insulin delivery systems that combine continuous glucose monitors (CGM) and insulin pumps, minimizing or preventing hypoglycemic episodes and variability of blood sugar levels. After a few

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—JANICE HWANG, MD, MHS

months, she will test their brains again to see if they light up the way they should.

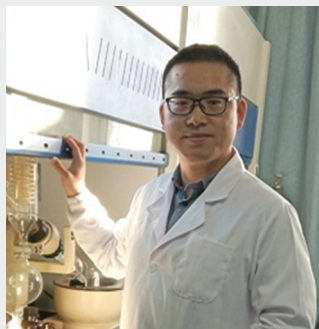
In the meantime, she says, it’s important for patients to have open conversations with their health care teams about hypoglycemia. “Doctors spend so much time getting A1C down, they don’t spend enough time addressing people’s fears of hypoglycemia,” she says. “And that’s the root cause of a lot of patients’ problems with adherence.”

# Achieving Full Autonomy

Working on the next generation of glucose monitoring

## Bing Wang PhD

By Andrew Curry



When continuous glucose monitors (CGM) were introduced more than 20 years ago, they represented a huge leap forward in diabetes care. The devices offered people with diabetes a way to monitor their glucose levels in near-

real time, without the hassle of pricking their fingers multiple times a day to get a reading from a blood glucose meter.

Research soon showed that CGMs offered people with both type 1 and type 2 diabetes significantly improved blood sugar (blood glucose) management. The devices were particularly helpful for kids, simplifying the daily routine of monitoring their blood sugar. Yet two decades later, only 33 percent of Americans with type 1 diabetes use a CGM, along with just 10 percent of people with type 2.

The reasons more people don't use the devices vary. In a 2018 study published in the journal *Clinical Diabetes*, researchers found that 37 percent of adult CGM users stopped using them because they had to replace the sensors too often. A similar percentage said they needed to be calibrated too often, requiring frequent, painful finger sticks.

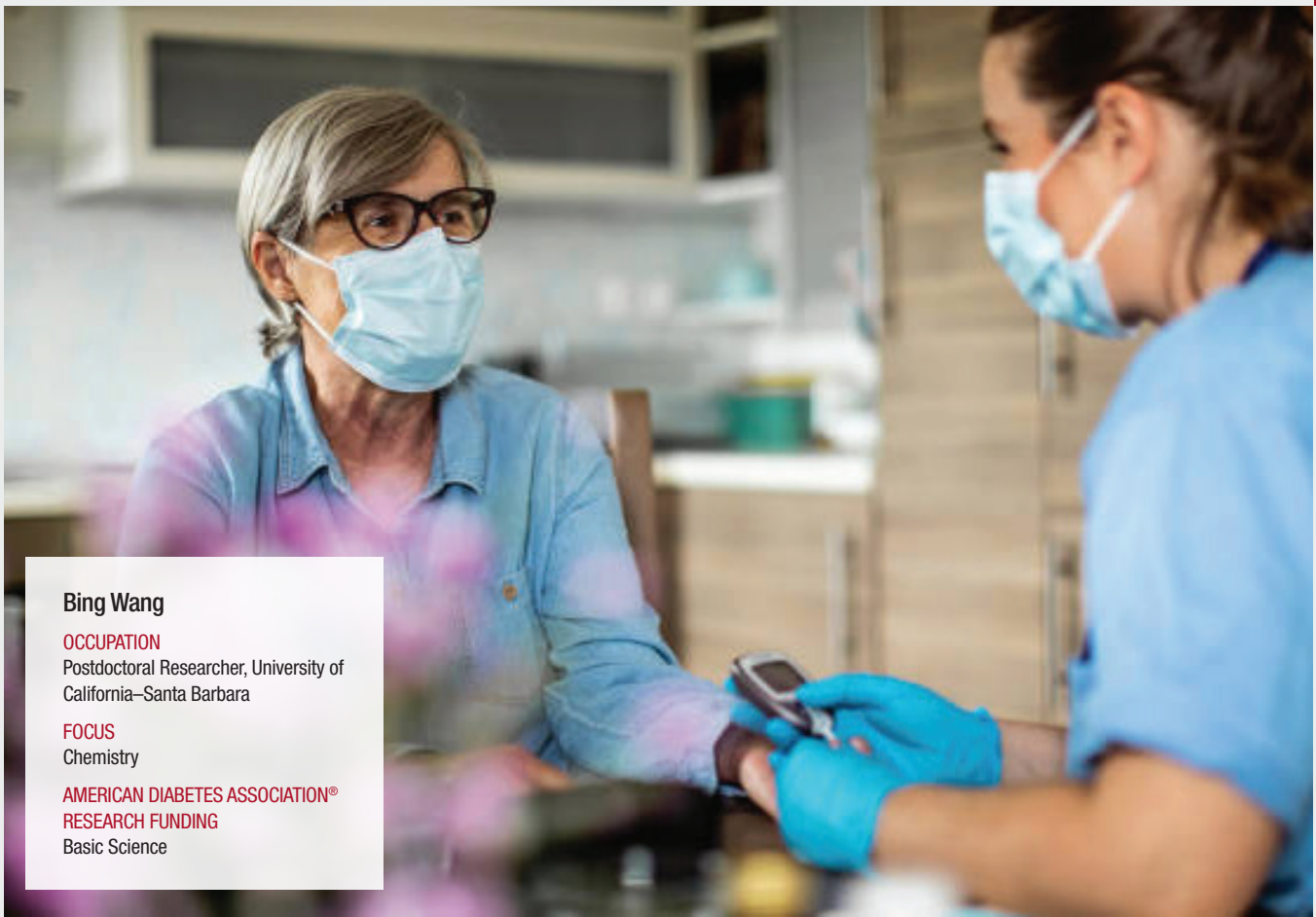
Among parents of children with type 1 diabetes, almost 40 percent said their children found CGMs painful to use.

University of California–Santa Barbara chemist Bing Wang, PhD, is looking for ways to change that. He says **CGM use could go up, helping people better manage their diabetes, if the devices were easier to use, less obtrusive, and required fewer finger sticks to calibrate.**

With the help of a grant from the American Diabetes Association, Wang is searching for ways to tweak cutting-edge CGMs to make them ultra-stable. His hope is to find a sensor setup that won't need to be calibrated as often, or at all.

With the standard CGM setup, that's a challenge. Almost all CGMs on the market work the same way: When a beneath-the-skin sensor comes in contact with glucose in the body, a chemical reaction creates an electrical signal. The tiny pulse of electricity, in turn, is carried along a wire to the CGM's transmitter and transformed into a glucose reading by a tiny computer in the monitor.

Such sensors have become so reliable that many CGMs now come "factory calibrated" and typically don't need daily finger sticks to fine-tune to the body chemistry of individual users. But because the sensitive chemicals coating the sensor don't last, the sensors have to be replaced regularly. "Enzyme-based sensors are only effective for two weeks at most," says Wang. Some need to be replaced as often as



### Bing Wang

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#### AMERICAN DIABETES ASSOCIATION®

#### RESEARCH FUNDING

Basic Science

weekly. That can get pricey, often costing hundreds of dollars for a month's supply even if you have insurance coverage.

That's why Wang is interested in the potential offered by a new type of sensor. First introduced to the market in 2018 under the brand name Eversense, the so-called optical sensor is embedded in a tiny implant that's inserted just beneath the skin. It relies on chemicals that let off a tiny flash of light when they come into contact with glucose, and it translates the intensity of the light into a glucose reading. The implant (along with its sensors) stays under the skin for as long as six months, charging and communicating via a removable transmitter.

Wang says the Eversense comes with a drawback of its own: Perhaps because of the way the light sensors work or the underlying chemistry of the sensor substances, the manufacturer still recommends that users calibrate the reader every 12 hours using finger sticks and a blood glucose meter.

When he first heard about the Eversense technology, Wang wondered whether the optical sensor could be tweaked. "How can we reduce or remove the requirement for the finger stick?" he asks. "In other words, how can we make the optical sensor more stable?"

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**“HOW CAN WE REDUCE OR REMOVE THE REQUIREMENT FOR THE FINGER STICK? IN OTHER WORDS, HOW CAN WE MAKE THE OPTICAL SENSOR MORE STABLE?”**

—BING WANG, PHD

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He hopes to identify a chemical reporter that won't need to be calibrated as often, or at all. The work is a long way from human application, but it could be an important building block for future generations of sensors. "It's still fundamental research," he says. "I'm changing the optical properties of the reporter and monitoring what happens."

Wang's work is inspired by a colleague whose daughter has type 1 diabetes, and he says easier-to-use CGMs would benefit people with type 2 as well. He's hopeful his research will someday make a difference that people with diabetes can feel every day. "It's important to reduce the panic around finger sticks for these kids," he says. "If we don't need finger sticks, we'd reduce the pain and fear associated with CGMs."

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# 2020 COVID-19 Research Awardees

When the COVID pandemic swept the world, ADA jumped into action, issuing a request for applications for 1 year, \$100,000 grants to study how COVID affects people with diabetes. Operating on an aggressive timeline, the announcement was issued, over 200 grant applications were received, and the applications were quickly but thoroughly reviewed. The 10 highest-scoring applications were awarded funding starting July 1. Final results will be reported in July 2021.



## Understanding immune and clinical causes of diabetes-related risk in COVID-19

**Carla J. Greenbaum, MD**

**Institution:** Benaroya Research Institute at Virginia Mason  
**Diabetes Type:** Both type 1 and type 2 diabetes  
**Program Area:** Immunology

**PROJECT DESCRIPTION:** The aim of this project is to understand, as widely reported, **why people with type 2 diabetes appear to be particularly impacted by the COVID-19 pandemic.** People with type 2 diabetes who are infected with COVID-19 are more likely to suffer complications. They are more likely to be hospitalized, be placed in intensive care units (ICU), have to use a ventilator and are less likely to survive their infection than those without type 2 diabetes. We will study how the immune system's response to infection differs among individuals infected with COVID-19 who do and do not have type 2 diabetes. We will also try to understand if these differences are part of the type 2 disease process itself. A further goal is to understand why some, but not all, people with type 2 diabetes have a worse outcome than others.

**GOAL:** We hope that this understanding will help clinicians target specific risk factors for treatment or suggest the most effective therapies to combat the consequences of COVID-19 infection in people living with type 2 diabetes.



## Colchicine/statins for the prevention of COVID-19 complications in diabetic patients (colstat-dm) trial

**Alexandra Lansky, MD**

**Institution:** Yale University School of Medicine  
**Diabetes Type:** Type 2 diabetes  
**Program Area:** Clinical Therapeutics/New Technology

**PROJECT DESCRIPTION:** This project aims to determine whether COVID-19 complications in hospitalized patients with diabetes could be prevented with a combination of colchicine and statins in addition to standard of care.

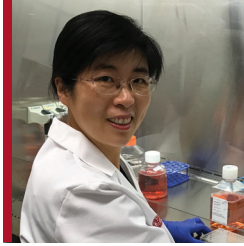
**GOAL:** We believe that a combined treatment of colchicine and statins has a synergetic effect to antagonize COVID-19 infection and modulate the inflammatory response, ultimately reducing the morbidity and mortality associated with acute respiratory distress syndrome (ARDS) and myocardial injury in COVID-19 patients.

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“As the COVID-19 pandemic is taking a high death toll, it is our overarching goal to find the best treatment of care for people with diabetes and contribute to the global effort of preventing COVID-19 complications and death.”

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“It is so gratifying to see decades of basic science research translating to improved health for people living with type 1 diabetes. With the knowledge that we can delay the onset of type 1 diabetes, the myriad of new therapies for type 2 diabetes, and the increasing use of technologies—research already impacts people with diabetes. While significant scientific, psychological, and health care delivery issues remain to be wrestled with, the commitment of the American Diabetes Association and researchers worldwide continue to move the needle to a better life for those with diabetes and their family members.”



## Determine the impact of COVID-19 infection on human pancreatic endocrine cells

Shuibing Chen, PhD

**Institution:** Joan & Sanford I. Weill Medical College of Cornell University

**Diabetes Type:** Both type 1 and type 2 diabetes

**Program Area:** Islet Biology/Apoptosis

**PROJECT DESCRIPTION:** This study seeks to explore what types of diabetes associated cells are infected and how those cells respond to COVID-19 infection. Recent clinical studies show a strong association between COVID-19 and diabetes. In the Diabetes Program of Surgery at Weill Cornell Medicine, we focus on studying the impact of genetic factors and environmental factors on pancreatic  $\beta$  cell generation, function, and proliferation in type 1 and 2 diabetes. There is an urgent need for physiological models to study SARS-CoV-2 infection using diabetes-relevant human cells. We have created a platform comprised of human pluripotent stem cells (hPSC)-derived endocrine cells. We found that human pancreatic alpha and beta cells are highly permissive to SARS-CoV-2 infection, further validated using adult primary human islets. SARS-CoV-2 infection caused striking expression of chemokines, similar to primary human COVID-19 pulmonary autopsies.

**GOAL:** To validate the SARS-CoV-2 infection using autopsy pancreatic samples from COVID-19 patients and systematically evaluate the impact of SARS-CoV-2 infection on human endocrine cells.

**PROGRESS TO DATE:** Dr. Chen and team continue to study the effects of the SARS-CoV-2 virus in human pancreatic cells. Their publication is pending and they presented initial data at February's Keystone Symposia—Diabetes: Many Faces of the Disease joint meeting with Obesity: From Cell to Patient.

“Diabetes is a complicated polygenic disease. We study how genetic and environmental factors contribute to diabetes progression, and our research goal is to facilitate the development of personalized therapy. This grant will allow us to explore the impact of SARS-CoV-2 infection on human endocrine cells.”



## Investigating beta cell survival, function, and metabolism during the pathogenesis of COVID-19

Senta K. Georgia, PhD

**Institution:** Children's Hospital Los Angeles

**Diabetes Type:** Both type 1 and type 2 diabetes

**Program Area:** Islet Biology/Apoptosis

**PROJECT DESCRIPTION:** This project focuses on the effects of COVID-19 on the function, survival and regeneration of insulin cells. There is a direct relationship between the number of insulin-secreting cells a person has and their capacity to maintain healthy blood sugar levels. We are trying to understand if having COVID-19 acutely injures insulin cells and if these cells are able to recover from COVID-induced injury. This information is critical to understanding if a generation of people will develop diabetes as a result of the COVID-19 pandemic. We will use experimental methods to detect insulin cell injury during a period where someone has the COVID-19 disease.

**GOAL:** If we can detect active insulin cell injury and understand how COVID-19 is inflicting this injury, then we can devise strategies to protect insulin cells from injury or help them recover after patients have won their battle against COVID-19.

“The fact that my research contributes fundamental insights that will lead to the monumental discovery, i.e. a cure for diabetes, keeps me motivated to work every day. I work for my grandmother, who has diabetes. I work for my students' families who have diabetes. I work for the children seen in our clinics at Children's Hospital Los Angeles who have diabetes. And I work for all of the people I don't know who have diabetes.”

### DISCLAIMER:

All project descriptions were submitted from the scientists.



## Prognostic biomarkers for severity of disease in COVID-19 and metabolic syndrome

Joshua L. Denson, MD

Institution: Tulane University

Research Type: Obesity

Program Area: Obesity/Pathogenesis

**PROJECT DESCRIPTION:** The study focuses on the relationship between metabolic syndrome, diabetes, obesity, and COVID-19. Emerging data suggest high risk groups may exist such as those with obesity and diabetes, yet clinical trials have not begun targeting these at-risk patients due to the need for further research. Obesity, diabetes, hypertension and hyperlipidemia make up the essential components of metabolic syndrome, and are extremely prevalent in the American population, particularly in Louisiana. One out of every three (36.8%) residents are considered obese, ranking Louisiana among the top 10 states for adult obesity. Similar numbers are seen for diabetes, with almost 12% (more than 500,000) of Louisiana residents aware that they have diabetes and another 5% with prediabetes.

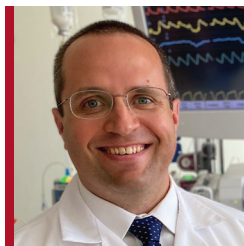
A subset of COVID-19 patients are at risk for developing severe disease, often resulting in lung inflammation. Obesity, diabetes and metabolic syndrome are associated with a chronic low-grade inflammation predominantly manifested in elevated serum biomarker levels. Additionally, we know that acute respiratory distress syndrome (ARDS), the most common

“Diabetes is a disease that has personally affected many of my immediate family members and continues to be an ongoing issue in my life. As a physician-scientist working in the ICU, I have seen firsthand the effects of COVID-19 and who this disease affects the most. This award will be a launching point for my research efforts into COVID-19 and metabolic disease with the hope to continue to learn and help those suffering from these disease processes.”

manifestation of severe COVID-19, is associated with a similar inflammatory biomarker profile. Thus, there is a critical need to determine the prognostic value of these biomarkers in COVID-19 patients presenting with ARDS and metabolic syndrome.

**GOAL:** To have identified metabolic syndrome as a risk factor for severe disease in COVID-19, as well as the nature of the inflammatory profile predisposing these patients to worse outcomes. These results are expected to have an important, positive impact on precision treatment strategies by identifying a group of patients who may benefit from early intervention, particularly those with metabolic syndrome and diabetes.

**PROGRESS TO DATE:** Dr. Denson and team reported one peer-reviewed publication resulting from work supported by this grant on the clinical characteristics and outcomes of people hospitalized with COVID. They continue to support the association of metabolic syndrome and COVID-19 severity.



## Metabolic contributions to multiple organ failure in diabetic patients with COVID-19

Michael David Maile, MD

Institution: Regents of the University of Michigan

Diabetes Type: Type 2 diabetes

Program Area: Integrated Physiology/Fatty Acid Metabolism

**PROJECT DESCRIPTION:** This project will investigate why COVID-19 affects people with diabetes more severely than those without diabetes. To better understand why this occurs, we will measure hundreds of metabolites and inflammatory proteins in serial samples

“As a critical care physician, I routinely care for extremely sick patients, many of whom have diabetes. Our lack of specialized treatments for patients with diabetes is frustrating as a clinician and makes it particularly important for me to conduct diabetes research.”

collected over time from patients hospitalized with COVID-19. Differences between patients with and without a history of diabetes will be used to identify the pathways that produce this effect.

**GOAL:** Uncovering the underlying mechanisms will allow us to work on developing targeted therapies to improve the care of patients with diabetes suffering from COVID-19.

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**Help Support Diabetes Science.** If you would like to support diabetes research, please go to [diabetes.org/researchdonation](https://diabetes.org/researchdonation)

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### **COVID-19: role of adipose tissue**

**Tracey Lynn McLaughlin, MD**

**Institution:** The Board of Trustees of the Leland Stanford Junior University

**Research Type:** Obesity

**Program Area:** Obesity/Clinical Treatment

**PROJECT DESCRIPTION:** This project addresses the **link between severe COVID-19 disease and obesity/diabetes.**

Specifically, ACE2, the receptor for the spike protein on COVID-19, is highly expressed in subcutaneous and visceral adipose tissue, which may allow for viral entry and replication. Particularly in peri-organ fat depots, inflammation, vasoconstriction and fibrosis as a consequence of viral infection and downregulation of ACE2 may contribute to organ damage including, the heart, gut, liver and kidneys.

**GOAL:** The goal of this project is to determine whether SARS-CoV-2 infects human adipocytes from subcutaneous (SAT), visceral (VAT) and epicardial adipose tissue (EAT), whether infection incites inflammation and whether pharmacologic compounds that target the renin-angiotensin system (RAS)/ACE2 alter infectivity and inflammation.

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“ I study diabetes and obesity and feel compelled to address the obesity link since it has been identified as the strongest risk factor, besides age, for severe COVID-19. I study human fat cells/tissue and have access to cultivated virus and BSL3 where we can infect cells with SARS-CoV-2, making our group uniquely capable of addressing this question.”



### **Characterize the host immune responses in subjects with or without COVID-19 and/or diabetes**

**Zhi Q. Yao, MD, PhD**

**Institution:** East Tennessee State University

**Diabetes Type:** Both type 1 and type 2 diabetes

**Program Area:** Immunology

**PROJECT DESCRIPTION:** This study is meant to characterize the innate and adaptive immune responses in subjects with or without COVID-19 and/or diabetes to **have a better understanding of the impact of diabetes on COVID-19, and visa versa.**

**GOAL:** The purpose is to gain fundamental insights into their immunological profiles to guide future management of patients with COVID-19 and its complications with or without diabetes.

**PROGRESS TO DATE:** Dr. Yao and team reported two peer-reviewed publications resulting from the work supported by this grant. They are actively working on identifying virus-specific T cell and B cell epitopes in COVID-19 research subjects.

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“ The future of diabetes research will enable us to know more about prevention and treatment of both type 1 and type 2 diabetes, but this goal can only be achieved through scientific research supported by professional associations, physicians, scientists, and patients! We have to work together to fight diabetes and infectious diseases like COVID-19.”

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### Using genetics to identify causal cardiometabolic risk factors of COVID-19 severity and diabetes-related complications in COVID-19

Aaron S. Leong, MD, MSc

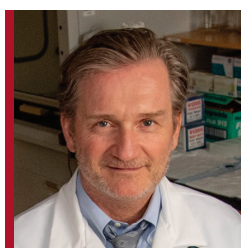
**Institution:** Massachusetts General Hospital  
**Diabetes Type:** Both type 1 and type 2 diabetes  
**Program Area:** Epidemiology

**PROJECT DESCRIPTION:** This project aims to examine the relationship between diabetes genetics and life-threatening complications of COVID-19 illness. We seek to **determine whether genetics can explain why some people with diabetes experience a more severe clinical course of COVID-19 than others.**

**GOAL:** We hope that this project will identify diabetes-related risk factors for COVID-19. By identifying genes and biological pathways related to COVID-19 severity and diabetes-related complications, we may target them therapeutically to reduce the risk of severe COVID-19 illness.

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“I have always wanted to do more for my patients and for people with diabetes around the world. My patients teach me about diabetes, which informs my research. This award supports my overall research focus in the application of diabetes genetics to precision medicine and public health.”



### Role of sex, metabolic disease and inflammation in COVID-19 severity

Franck Mauvais-Jarvis, MD, PhD

**Institution:** Tulane University  
**Research Type:** Obesity  
**Program Area:** Obesity/Pathogenesis

**PROJECT DESCRIPTION:** This project is conducted to gain a better understanding of **the role of type 2 diabetes, obesity and metabolic syndrome, as well as male biological sex and race, particularly in non-Hispanic Black men**, in increasing COVID-19 severity and mortality.

**GOAL:** Understanding why non-Hispanic Black men with type 2 diabetes, who are obese and have metabolic syndrome are at a greater risk of COVID-19 mortality is important. It will provide novel approaches for the development of personalized diagnosis tests, as well as health monitoring and preventive precision medicine strategies.

**PROGRESS TO DATE:** Dr. Mauvais-Jarvis and team reported two peer-reviewed publications resulting from their grant-supported work to characterize the factors that increase the risk for severe COVID-19 outcomes. They continue to look at sex differences in blood inflammatory markers and immune cells in relation to severe outcomes.

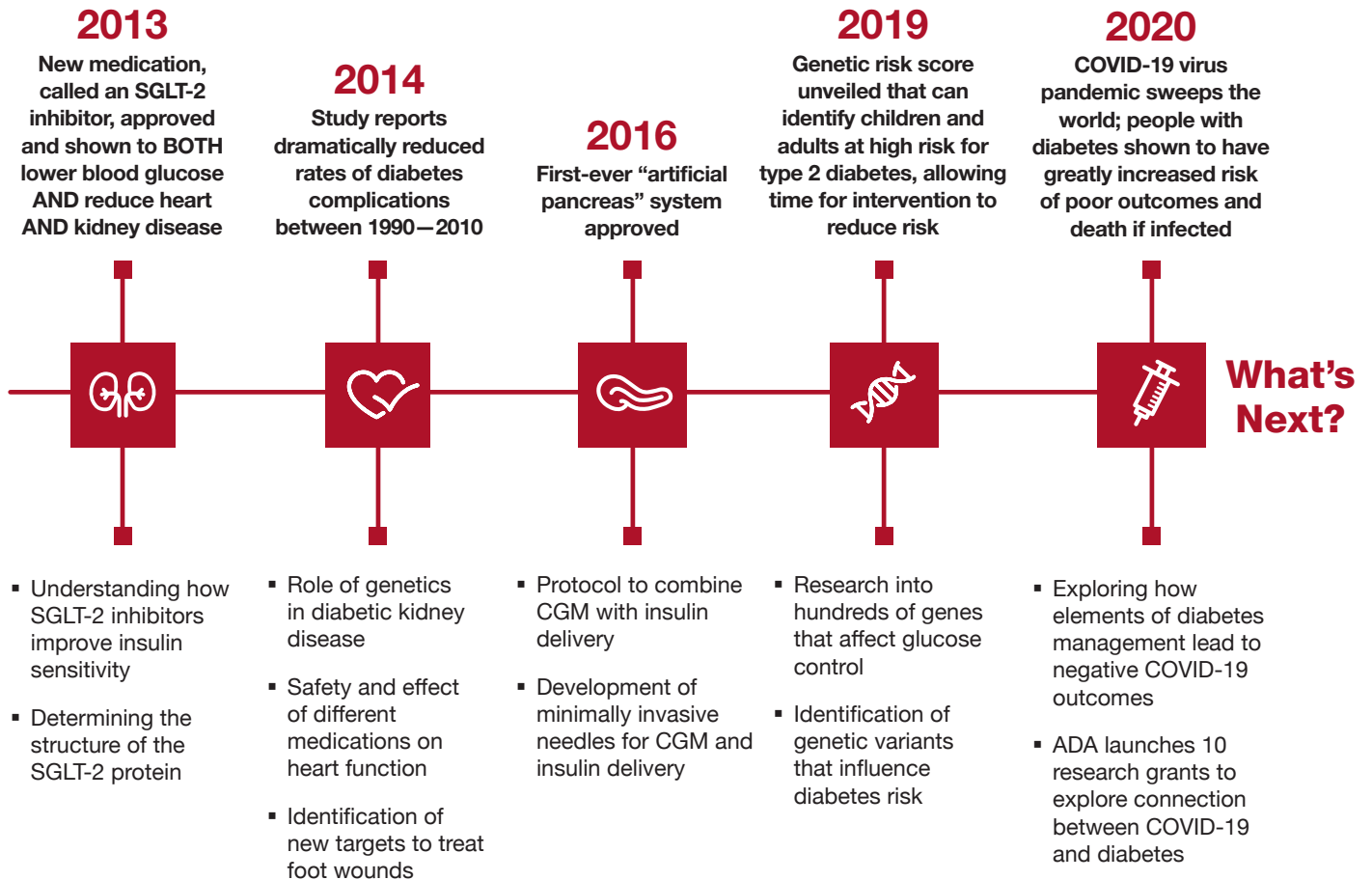
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“I have spent my research career trying to understand the mechanism of type 2 diabetes and find new therapeutic approaches. This award will open a new avenue of research in my effort to better understand the effect of diabetes and obesity on COVID-19 severity.”



# On the Road to a Cure

Research for Life



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# Innovation

 American  
Diabetes  
Association®  
Research Foundation

**Pathway to  
Stop Diabetes®**

The Pathway to Stop Diabetes® initiative was founded in 2013 with a singular vision: to introduce a new generation of brilliant scientists to diabetes research. The ADA supports Pathway scientists for five to seven years, giving them the freedom to explore new ideas without the constraints of traditional project-based funding.

## PATHWAY PRODUCTIVITY

Since its inception, our Pathway researchers collectively:

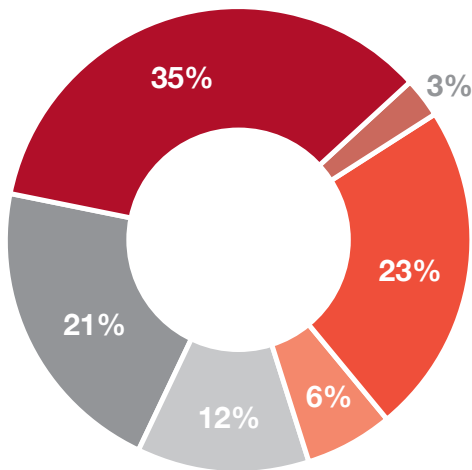
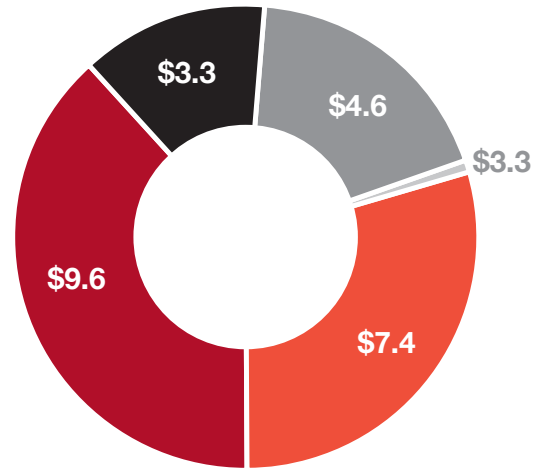
- Published **170 original research manuscripts based on their Pathway work**
- Applied for **8 patents**
- Delivered **204 presentations and 264 lectures**

# 2020 Research Funding

## Grant Type

(dollars in millions)

- Core Research
- Core Development
- Core Training
- Collaborative targeted
- Pathway to Stop Diabetes



## Diabetes Type

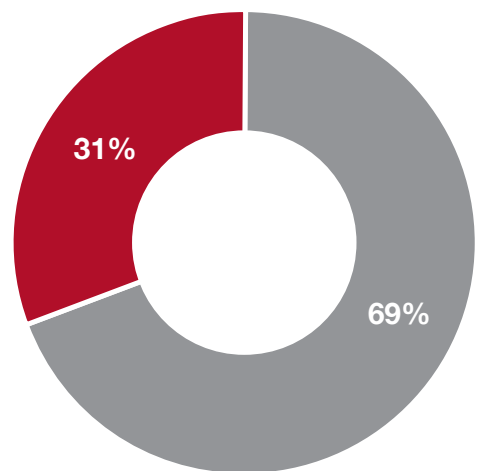
(percent of dollars)

- T1D
- Both Type 1 and Type 2
- T2D
- Gestational Diabetes
- Obesity
- Prediabetes/Insulin Resistance

## Research Type

(percent of dollars)

- Basic Science
- Clinical and Translational Science



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can't accomplish  
when we are  
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