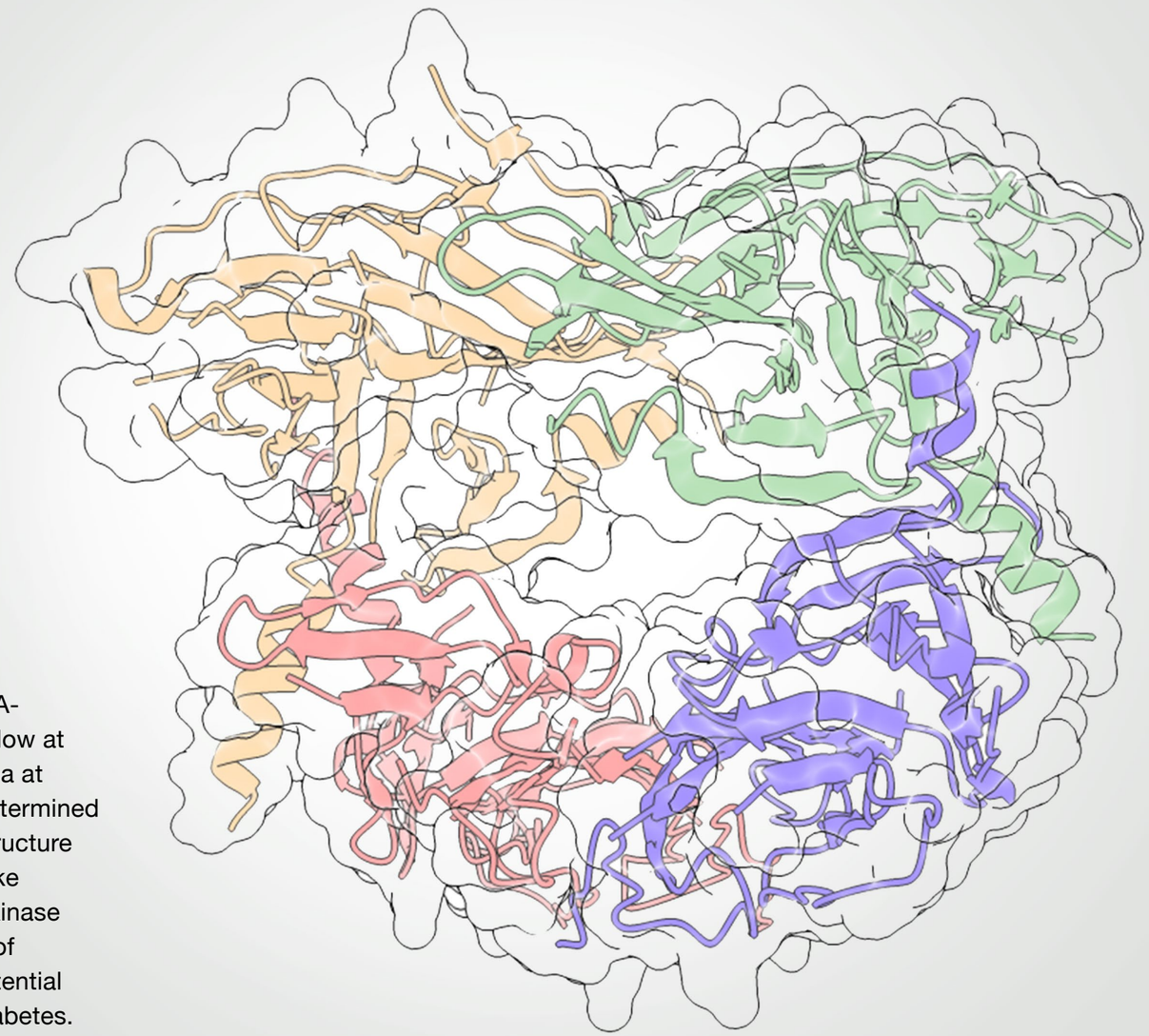
Innovating for Life.

American Diabetes Association®
Research Foundation

2019 Research Report

The American Diabetes Association® (ADA) Supports Innovative Diabetes Research



Jiahui Tao, PhD, an ADA-funded Postdoctoral Fellow at the University of Alabama at Birmingham, recently determined the atomic-resolution structure of protein kinase RNA-like endoplasmic reticulum kinase (PERK), a key regulator of insulin secretion and potential therapeutic target for diabetes.

Credit/Source: Jiahui Tao

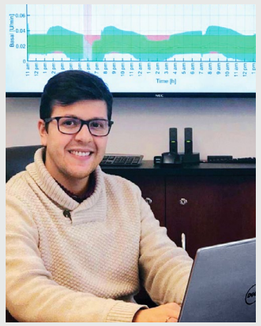
Contents

Cover: ADA-funded scientist Nora Kory, PhD, conducting diabetes research at Massachusetts Institute of Technology.

Diabetes Research is Personal for Two ADA-funded Scientists

José García-Tirado, PhD

The Rector and Visitors of the University of Virginia | Postdoctoral Minority Fellowship



"Receiving an ADA Postdoctoral Minority Fellowship award marks an inflection point in my career since it signifies the beginning of my time as an independent scientist. This award will enable me to pursue my own ideas as I work to become a leader in the field of diabetes technology."

For people with diabetes and dependent on insulin, each day involves a delicate balancing act to control blood glucose levels. ADA-funded researcher Dr. José García-Tirado is one of the 7 million people living in the United States that are dependent on insulin to live. He was diagnosed with type 1 diabetes over six years ago, in the middle of 2013.

Dr. García-Tirado received his training in the discipline of Control Engineering, which is a field that broadly seeks to use technology to automate different processes. Although he had no background in diabetes research, he knew he could use his engineering skills to reduce the burden of diabetes and improve the lives of people living with diabetes, including his own. "Soon after my diagnosis, I discovered the exciting world of diabetes technology and, as a Control Engineer, seized the perfect opportunity to contribute to the advancement of the field from my professional skills," explained Dr. Garcia-Tirado.

Until recently, people with diabetes were forced to deal with constant finger pricks and insulin injections to manage their glucose levels. Technology has come a long way over the past few decades to reduce the burden of diabetes management. Since the introduction of the first commercial continuous glucose monitor and insulin pump, fewer people with diabetes require finger sticks and insulin injections. Still, the mecca of diabetes technology, the fully-automated artificial pancreas, remains out of reach.

Dr. García-Tirado's ADA-funded research project is working to make the fully-automated artificial pancreas a reality. The idea of the artificial pancreas is to combine an insulin pump and continuous glucose monitor into a single entity, in which readings captured by the glucose monitor determine how much insulin is dispensed by the pump. No user decisions would be required.

Currently, only a semi-automated artificial pancreas exists. That means users still must determine how many carbohydrates they are about to consume before a meal, calculate the appropriate corresponding insulin dose, and administer it. Dr. García-Tirado's ADA-funded research aims to change this. His plan is to collect data regarding patients' meals, which he can then use to generate a tailored eating pattern for each individual person. This tailored pattern can then be fed into one of the most advanced control structures available nowadays to perform the best decision making about the insulin dose to be applied before, during and after every meal, effectively eliminating the need for carbohydrate counting.

"In plain words, once our approach succeeds, people with type 1 diabetes using an artificial pancreas will be relieved from the burden of counting carbohydrates and announcing meals in different daily scenarios," explained Dr. García-Tirado.

Maurice B. Fluitt, PhD

Georgetown University | Postdoctoral Minority Fellowship

"It is my hope to become a leading diabetes investigator and conduct groundbreaking research that unravels the complex mystery of diabetic kidney disease. My ADA award will be instrumental in making this dream a reality."

Diabetes affects 1 in 11 people, with a new person diagnosed every 21 seconds. Even though diabetes can lead to serious complications, it's easy to assume that diabetes isn't that big of a deal. You see people in public checking their blood glucose or giving themselves an insulin injection, and perhaps for people on the outside, it doesn't seem that bad. Of course, those dealing with the burden of diabetes, whether personally or as a loved one, know that diabetes can affect you physically, mentally and emotionally.

For ADA-funded researcher Dr. Maurice Fluitt, the seriousness of diabetes is all too real. Growing up, his father had type 2 diabetes. Despite his diagnosis, Dr. Fluitt's father continued to thrive. It was only after developing diabetic kidney disease and going on dialysis for treatment that things changed.

"My Dad was told by a physician that most dialysis patients only survive five years after being placed on treatment. I will never forget that moment because it literally shifted our entire family structure. My Dad, who was full of life and personality suddenly became a shell of himself. And as much as he tried to 'shake off' the weight of dialysis treatment, he couldn't," explained Dr. Fluitt. "Five years later, on a cold December day, my Dad passed away due to end stage kidney failure."

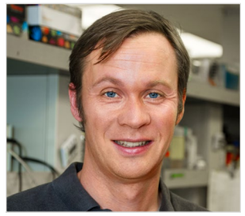
Dr. Fluitt has used his personal experience with diabetes as motivation. He has chosen to dedicate his career to help ensure future advances that will improve outcomes for people dealing with diabetes and its complications. "Research has always been a beacon of hope for me. I know my father would be proud of the work that I'm doing."

Last year, Dr. Fluitt received an ADA Postdoctoral Minority Fellowship award, sponsored by the Fineberg Foundation, to conduct research on diabetic kidney disease at Georgetown University. His project is focused on identifying biomarkers that are easily detectable and could be used to identify people with diabetic kidney disease earlier than traditional methods. If successful, his research may lead to a day when diabetic kidney disease could be detected when it's progression could still be significantly delayed or reversed. His research is also looking into new targets that could lead to new and better treatments.

Every year, there are estimated to be more than 50,000 new cases of diabetic kidney disease, and a quarter million people are currently living with kidney failure related to diabetes. One in four people with diabetes are living with some degree of impaired kidney function. That's why research like Dr. Fluitt's is so important.

"This is an exciting time for diabetes research, and specifically the field of diabetic kidney disease. I am confident that with sustained research, we will one day be able to live in a world without this devastating diabetes complication."

Advances From ADA-funded Researchers—Type 1 Diabetes

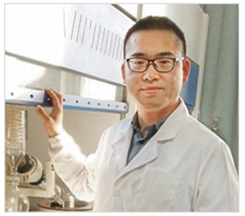


Identification of a new player in type 1 diabetes risk

Thomas Delong, PhD
University of Colorado, Denver
Pathway to Stop Diabetes award
Funded for 5 years at
$325,000 per year

Type 1 diabetes is caused by an autoimmune attack of insulin-producing beta-cells. While genetics and the environment are known to play important roles, the underlying factors explaining why the immune system mistakenly recognize beta-cells as foreign is not known. Now, Dr. Delong has discovered a potential explanation. He found that proteins called Hybrid Insulin Peptides (HIPs) are found on beta-cells of people with type 1 diabetes and are recognized as foreign by their immune cells. Even after diabetes onset, immune cells are still present in the blood that attack these HIPs.

Next, Dr. Delong wants to determine if HIPs can serve as a biomarker or possibly even targeted to prevent or treat type 1 diabetes.

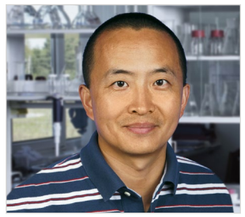


A novel molecule to improve continuous glucose monitoring

Bing Wang, PhD
University of California, Santa Barbara
Funded for 3 years at
$60,000 per year

To create a fully automated artificial pancreas, it is critical to be able to quantify blood glucose in an accurate and stable manner. Current ways of continuously monitoring glucose are dependent on the activity of an enzyme which can change over time, meaning the potential for inaccurate readings and need for frequent replacement or calibration. Dr. Wang has developed a novel molecule that uses a different, non-enzymatic approach to continuously monitor glucose levels in the blood. This new molecule is stable over long periods of time and can be easily integrated into miniaturized systems.

Now, Dr. Wang is in the process of patenting his invention and intends to continue research on this new molecule so that it can eventually benefit people living with diabetes.



A new way to prevent immune cells from attacking insulin-producing beta-cells

Jianxun Song, PhD
Texas A&M University System Health Science Center
Funded for 3 years at
$115,000 per year

Replacing insulin-producing beta-cells that have been lost in people with type 1 diabetes is a promising strategy to restore control of glucose levels. However, because the autoimmune disease is a continuous process, replacing beta-cells results in another immune attack if immunosorbent drugs are not used, which carry significant side-effects. This year, Dr. Song reported on the potential of an immunotherapy he developed that prevents immune cells from attacking beta-cells and reduces inflammatory processes. This immunotherapy offers several potential benefits, including eliminating the need for immunosuppression, long-lasting effects, and the ability to customize the treatment to each patient.

The ability to suppress autoimmunity has implications for both prevention of type 1 diabetes and improving success rates of islet transplantation.

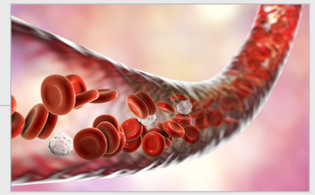
2019 Awardee Research Profile

Dr. Karen Cerosaletti from Benaroya Research Institute in Seattle, Washington received an **Innovative Clinical or Translational Science award** to study the underlying causes of the autoimmune attack that leads to type 1 diabetes.

> "My interest is understanding how the immune system malfunctions in type 1 diabetes so that we can more accurately predict who will develop type 1 diabetes, when they will develop it, and how we can prevent or block disease onset or progression. My ADA award will allow us to determine the role of T cells of the immune system in destroying pancreatic islets, resulting in loss of insulin secretion. Specifically, my project will investigate if a unique subset of islet T cells are present in the very early stages of development of type 1 diabetes, and if these unique cells accompany the loss of insulin secretion in newly diagnosed patients, suggesting a direct role in disease development and progression."

Notable innovations and discoveries since the ADA was founded

1941
Tablets for testing glucose levels from a urine sample become available



1948
High levels of blood glucose linked to vascular disease

1955
First oral medication for diabetes becomes available to treat certain types of monogenic diabetes and type 2 diabetes

1959
Distinct types of diabetes identified as a result of the research from Nobel prize winner Dr. Rosalyn Yarrow

Advances From ADA-funded Researchers—Type 2 Diabetes

A new target to improve insulin sensitivity

Scott Summers, PhD
University of Utah | Funded for 3 years at $200,000 per year

The hormone insulin normally acts like a 'key', traveling through the blood and opening the cellular 'lock' to enable the entry of glucose into muscle and fat cells. However, in people with type 2 diabetes, the lock on the cellular door has, in effect, been changed, meaning insulin isn't as effective. This phenomenon is called insulin resistance. Scientists have long sought to understand what causes insulin resistance and develop therapies to enable insulin to work correctly again. This year, Dr. Summers determined an essential role for a molecule called ceramides as a driver of insulin resistance in mice. He also presented a new therapeutic strategy for lowering ceramides and reversing insulin resistance. His findings were published in one of the most prestigious scientific journals, *Science*.

Soon, Dr. Summers and his team will attempt to validate these findings in humans, with the ultimate goal of developing a new medication to help improve outcomes in people with diabetes.

Determining the role of BPA in type 2 diabetes risk

Todd Hagobian, PhD
California Polytechnic State University
Funded for 3 years at $200,000 per year

Many synthetic chemicals have infiltrated our food system during the period in which rates of diabetes has surged. Data has suggested that one particular synthetic chemical, bisphenol A (BPA), may be associated with increased risk for developing type 2 diabetes. However, no study to date has determined whether consumption of BPA alters the progression to type 2 diabetes in humans. Results reported this year by Dr. Hagobian demonstrated that indeed when BPA is administered to humans in a controlled manner, there is an immediate, direct effect on glucose and insulin levels.

Now, Dr. Hagobian wants to conduct a larger clinical trial including exposure to BPA over a longer period of time to determine precisely how BPA influences glucose and insulin. Such results are important to ensure the removal of chemicals contributing to chronic diseases, including diabetes.

Understanding the biology of body-weight regulation in children

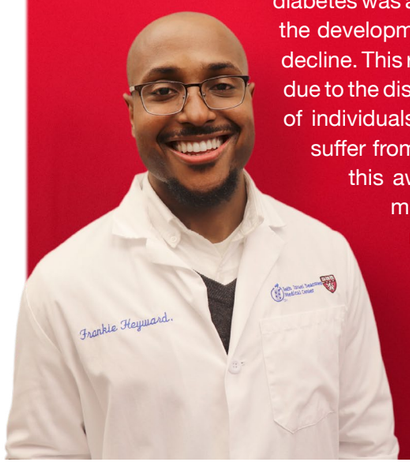
Ellen A. Schur, MD
University of Washington
Funded for 3 years at $200,000 per year

Determining the biological mechanisms regulating body-weight is important for preventing type 2 diabetes. The rise in childhood obesity has made this even more urgent. Behavioral studies have demonstrated that responses to food consumption are altered in children with obesity, but the underlying biological mechanisms are unknown. This year, Dr. Schur tested changes in brain and hormonal responses to a meal in normal-weight and obese children. Results from her study show that hormonal responses in obese children are normal following a meal, but responses within the brain are reduced. The lack of response within the brain may predispose them to overconsumption of food or difficulty with weight-loss.

With this information at hand, Dr. Schur wants to investigate how this information can be used to treat obesity in children and reduce diabetes.

2019 Awardee Research Profile

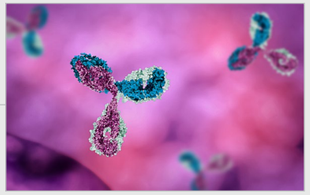
Dr. Frankie Heyward of Beth Israel Deaconess Medical Center in Boston, Massachusetts received a **Postdoctoral Minority Fellowship award** to research how the brain regulates food intake and energy balance.



"My research career focus was forged over a decade ago when I learned that type 2 diabetes was an independent risk factor for the development of age-related cognitive decline. This realization resonated with me due to the disproportionately high number of individuals within my community that suffer from type 2 diabetes. Receiving this award will ensure I make the most out of this phase of my postdoctoral training. My career-long research efforts will necessitate my being proficient in analyzing genetic data independently."

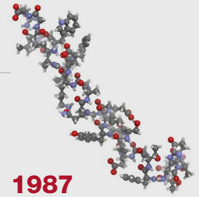
1970

Ames develops the first glucose meter that can be used in the clinic. Home glucose meters became available in 1981



1982

Autoantibody linked to type 1 diabetes discovered, helping scientists identify people at high risk prior to onset



1987

Hormone GLP-1 discovered, which plays an important role in the regulation of glucose levels

The New England
Journal of Medicine

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Volume 329 SEPTEMBER 30, 1993 Number 14

THE EFFECT OF INTENSIVE TREATMENT OF DIABETES ON THE DEVELOPMENT AND PROGRESSION OF LONG-TERM COMPLICATIONS IN INSULIN-DEPENDENT DIABETES MELLITUS

The Diabetes Control and Complications Trial Research Group*

Abstract *Background.* Long-term microvascular and neurologic complications cause major morbidity and mortality in patients with insulin-dependent diabetes mellitus. We tested the hypothesis that intensive diabetes therapy, the goal of maintaining blood glucose concentrations close to the normal range could decrease the frequency and severity of these complications.

Methods. A total of 1441 patients with IDDM — 726 in the secondary-intervention cohort and 715 in the primary-intervention cohort) and 715 with mild retinopathy (the secondary-intervention cohort) were randomly assigned to intensive therapy administered either with an external insulin pump or by three or more daily insulin injections and guided by the results of frequent blood glucose monitoring, compared with one or two daily insulin injections. The patients were followed for a mean of 6.5 years, and the appearance and progression of retinopathy and other complications were assessed regularly.

interval, 62 to 85 percent), as compared with conventional therapy. In the secondary-intervention cohort, intensive therapy slowed the progression of retinopathy by 54 percent (95 percent confidence interval, 27 to 72 percent) and reduced the development of proliferative or severe nonproliferative retinopathy by 47 percent (95 percent confidence interval, 14 to 67 percent). In the two cohorts combined, intensive therapy reduced the occurrence of microalbuminuria (urinary albumin excretion of >40 mg per 24 hours) by 39 percent (95 percent confidence interval, 21 to 52 percent), that of albuminuria (urinary albumin excretion of >300 mg per 24 hours) by 54 percent (95 percent confidence interval, 19 to 74 percent), and that of clinical neuropathy by 60 percent (95 percent confidence interval, 38 to 74 percent). The chief adverse event associated with intensive therapy was a two-to-threefold increase in severe hypoglycemia.

Conclusions. Intensive therapy effectively delays the

1993

Tight glucose control shown to reduce complications in type 1 diabetes

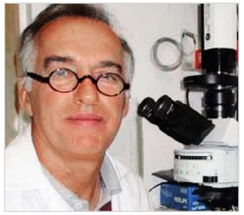
Advances From ADA-funded Researchers—Diabetes Complications

Addressing the legacy effect of diabetes

Neda Laiteerapong, PhD
The University of Chicago
Funded for 2 years at $138,000 per year

Several large clinical trials have demonstrated the importance of tight glucose control for reducing diabetes complications. However, few studies to date have tested this in the real-world, outside of a controlled clinical setting. In a study published this year, Dr. Laiteerapong found that indeed in a real-world setting, people with lower hemoglobin A1C levels after diagnosis had significantly lower vascular complications later on, a phenomenon known as the 'legacy effect' of glucose control. Her research noted the importance of early intervention for the best outcomes, as those with the low A1C levels just one-year after diagnosis had significantly lower vascular disease risk compared to people with higher A1C levels.

With these findings in hand, physicians and policymakers will have more material to debate and determine the best course of action for improving outcomes in people newly diagnosed with diabetes.



Identification of a potential therapy for diabetic neuropathy related to type 1 and type 2 diabetes

Nigel A. Calcutt, PhD
University of California, San Diego
Funded for 3 years at $200,000 per year

Diabetic neuropathy is a type of nerve damage that is one of the most common complications affecting people with diabetes. For some, neuropathy can be mild, but for others, it can be painful and debilitating. Additionally, neuropathy can affect the spinal cord and the brain. Effective clinical treatments for neuropathy are currently lacking. Recently, Dr. Calcutt reported results of a new potential therapy that could bring hope to the millions of people living with diabetic neuropathy. His study found that a molecule currently in clinical trials for the treatment of depression may be valuable for diabetic neuropathy, particularly the type affecting the brain.

Because the molecule is already in clinical trials, there is the potential that it can benefit patients sooner than later.

Investigating the loss of postmenopausal protection from cardiovascular disease in women with type 1 diabetes

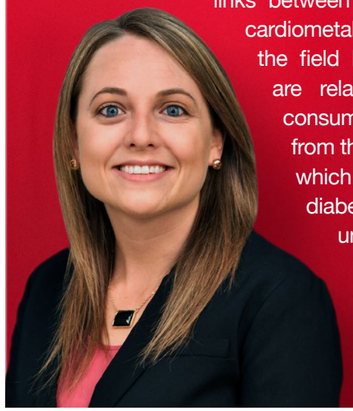
Janet K. Snell-Bergeon, PhD
University of Colorado
Funded 5 years at $170,000 per year

On average, women have a lower risk of developing heart disease compared to men. However, research has shown that this protection is lost in women with type 1 diabetes. The process of menopause increases rates of heart disease in women, but it is not known how menopause affects women with type 1 diabetes in regard to risk for developing heart disease. In a study published this year, Dr. Snell-Bergeon found that menopause increased risk markers for heart disease in women with type 1 diabetes more than women without diabetes.

Research has led to improved treatments and significant gains in life expectancy for people with diabetes and, as a result, many more women are reaching the age of menopause. Future research is needed to address prevention and treatment options.

2019 Awardee Research Profile

Dr. Joanne B. Cole of Massachusetts General Hospital in Boston, Massachusetts received a **Postdoctoral Fellowship award** to research how genetics and diet interact to affect diabetes risk.



"While we know diet and environment play a large role in diabetes, disentangling which specific dietary habits contribute to disease has been challenging. My ADA research project utilizes the genetics of dietary habits to make direct causal links between diet and diabetes and related cardiometabolic traits. Not only will this help the field better understand which genes are related to food preferences and consumption, we can also use the results from these genetic studies to determine which dietary habits directly cause diabetes and related traits. A better understanding of the roles diet and the genetics of diet play in diabetes will undoubtedly help prevent and treat diabetes."

2005

First medication in GLP-1 based class of therapies approved in the U.S., which was derived from the saliva of the Gila Monster

THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Changes in Diabetes-Related Complications in the United States, 1990–2010

Edward W. Gregg, Ph.D., Yanfeng Li, M.D., Jing Wang, M.D., Nilka Rios Burrows, M.P.H., Mohammed K. Ali, M.B., Ch.B., Deborah Rolka, M.S., Desmond E. Williams, M.D., Ph.D., and Linda Geiss, M.A.

ABSTRACT

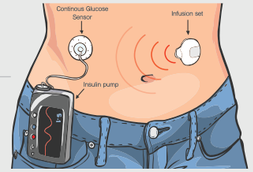
BACKGROUND

Preventive care for adults with diabetes has improved substantially in recent decades. We examined trends in the incidence of diabetes-related complications in the United States from 1990 through 2010.

METHODS

2014

Diabetes complications significantly reduced in the United States over the previous two decades



2016

The first semi-autonomous artificial pancreas becomes available

2018

Trials showing GLP-1 receptor agonists and SGLT-2 inhibitors significantly reduce heart disease rates in people with type 2 diabetes

Major Advances in Diabetes
Impacting Patients in 2019

By supporting scientists and the diabetes research they conduct, the American Diabetes Association plays a critical role in enabling transformational advances impacting the lives of people living with diabetes.

The problem: Diabetic kidney disease is a common complication of diabetes that has proven extremely difficult to prevent and treat.

The breakthrough: This year, a large clinical trial reported that an existing medication can slow progression and reduce mortality in people with diabetic kidney disease by more than 30%.

The problem: A class of medications called GLP-1 receptor agonists have helped people lose weight, improve glucose control, and reduce complications. However, these were only available as injectables.

The breakthrough: This year, a new medication was approved by the U.S. Food and Drug Administration (FDA) that enables the same tremendous benefits of this class of medications, but in pill form.

The problem: While identifying people at high risk for type 1 diabetes has become easier thanks to our understanding of the genetics, preventing or halting the autoimmune attack has remained challenging.

The breakthrough: This year, a study was unveiled showing an experimental immune therapy was able to delay diabetes onset by two years in children at high risk.

The problem: When a person with diabetes gets life-threatening low-blood sugar, caregivers can inject glucagon to raise blood sugar. However, the powdered glucagon must be reconstituted in a time-consuming process and dosage must be correctly calculated, wasting critical time.

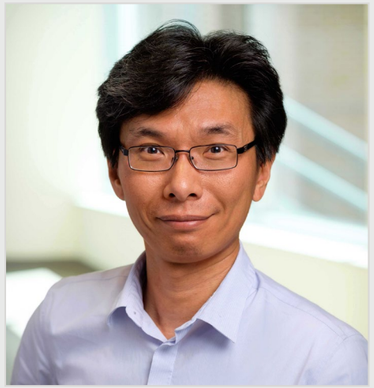
The breakthrough: This year, the FDA approved a new form of glucagon that can be administered as a nasal spray from a portable, single-use, ready-to-use device.

> "Fight 4 Diabetes Cure is proud to support the American Diabetes Association Research Foundation. Through our fundraising efforts we strive to help those who are living with diabetes now and those that will continue to be impacted by diabetes in the future. Our hope is that future generations will benefit from our continued efforts to help find a cure."
>
> **—Phil Cantor, Chairman | Fight 4 Diabetes Cure**

> "I have been proud to support diabetes research for the past 17 years so that my son-in-law can thrive and live the best life possible. ADA-funded researchers have contributed to significant advances that have improved his life and the lives of many people living with diabetes."
>
> **—Virginia B. Maloney, Richmond, Virginia**

The Impact of ADA-funded Research

ADA awards result in an average of nearly six publications, each cited nearly 30 times, expanding reach



"The publications produced through the support of the ADA funding increased my research productivity and will allow me to apply for other extramural funding. My ADA award also allowed me to initiate collaborations with other investigators with a common interest in the field of type 1 diabetes."

Yi-Guang Chen, PhD
Medical College of Wisconsin
Innovative Basic Science award funded 2016-2018

96% of researchers receiving an ADA award remain in diabetes research, ensuring talented scientists dedicate their careers to advances in diabetes

"Without my ADA award, I wouldn't be able to perform the proposed diabetes research and most likely, my career would have a different direction. My award and the resulting scientific achievements are a critical step forward in my career towards academia."

Monica Diaz-Coranguez, PhD
University of Michigan
Postdoctoral Minority Fellowship award funded 2016-2018

Each dollar the ADA invests in a researcher results in nearly $12.50 in subsequent research support from other sources

"I received my ADA award at a critical time, two years after my laboratory opened. This vote of confidence from the ADA helped me get other foundation awards and was a springboard for my first large NIH award."

Matthew J. Merrins, PhD
University of Wisconsin-Madison
Innovative Basic Science award funded 2016-2018

Each ADA-funded researcher mentors an average of four junior scientists who remain in the field of diabetes

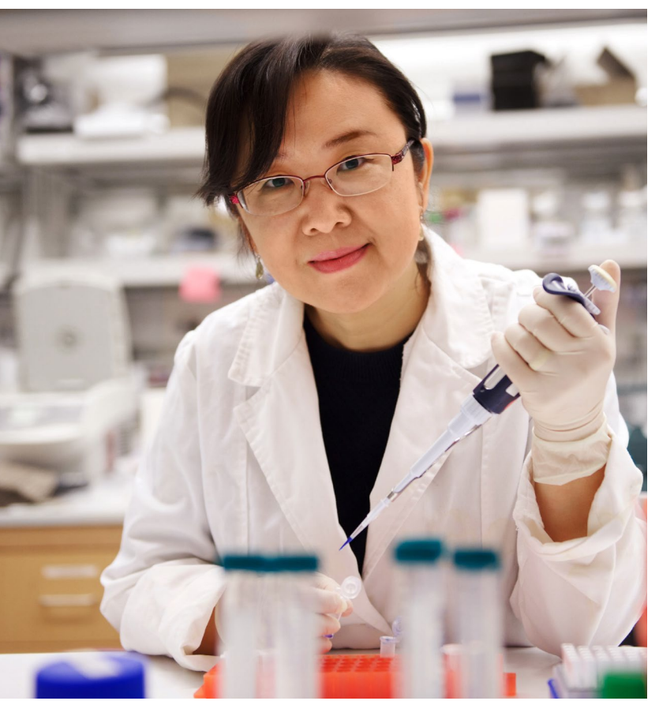
"My ADA project has allowed me to give a wealth of hands-on research experience to my trainees, which has enhanced their learning in immeasurable ways. I am so proud that several of my research mentees have moved on to either additional graduate training or to prestigious fellowships, and I am certain that the experiences they had with this project will resonate in their careers for years to come."

Briana M. Mezuk, PhD
University of Michigan
Innovative Clinical or Translational Science award funded 2016-2018, supported by The Kahlert Foundation

Behind ADA's Research Program

147
in-training or early career investigators supported in 2019

295
research projects supported in 2019



ADA-funded researcher Ling Yang, MD, PhD

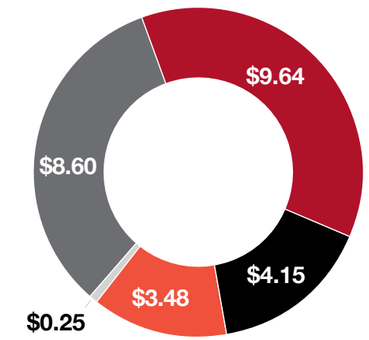
45
underrepresented minority researchers supported in 2019

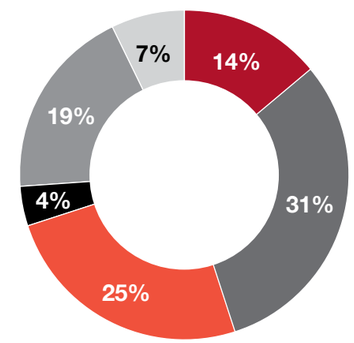
Supported diabetes research at
118
different institutions across the United States in 2019

2019 Research Funding

Grant Type
(dollars in millions)

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



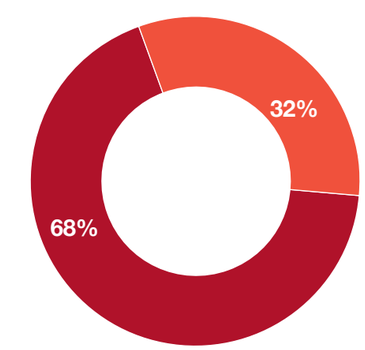


Diabetes Type
(percent of dollars)

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

Research Type
(percent of dollars)

- Basic Science
- Clinical and Translational Science



ADA-funded researcher Scott Summers, PhD (right)

Donate to Support Research

Today, scientists have unprecedented tools and technologies at their disposal. However, diabetes research is critically underfunded, leading to slower progress than may be possible if funding matched the scope of the epidemic.

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