2018 RESEARCH REPORT

COMMITTED TO RESEARCH BREAKTHROUGHS FOR_LIFE

American Diabetes Association®
Research Foundation

FOR_LIFE

The ADA is committed to supporting research to improve the lives of people with diabetes.

A Red Strider smiles for the camera at an ADA Step Out: Walk to Stop Diabetes event.

PATRICK'S STORY: THRIVING WHILE MANAGING DIABETES

Patrick Swingle is a typical American kid. He enjoys hanging out with his friends, playing rugby, rock climbing and going on backpacking trips. Patrick also has type 1 diabetes (T1D).

Rather than feel sorry for himself and let his diagnosis hold him back, he is thriving. "Patrick has completely integrated diabetes into who he is. It does not define him, but it is absolutely a part of him," stated his mother, Vivian.

Getting to this point wasn't a walk in the park, for either Patrick or his parents. "When Patrick was first diagnosed, our biggest concern was his blood sugar when he wasn't with us. Particularly when he was playing sports or at a friend's house. Sleeping was another big area of worry. We would test his glucose at midnight and again at 3 AM, but there were many nights when we would tip toe into his room, wearing a headlamp and saying a prayer that he'd still be breathing." The decision to adopt and trust the latest technological breakthroughs in diabetes management helped to ease this anxiety.

Just 3 months after his diagnosis, Patrick began using a pump to administer his life-saving insulin. Two years later, he was using continuous glucose monitoring to track his glucose levels throughout the day. "There is always an undercurrent of worry when you have a child with T1D, but glucose monitoring makes that undercurrent much quieter. Knowledge is power – and the access to his blood sugar levels gives us the information we need to support him as needed. Without that information, we lean more into worry and concern."

When Drs. Fredrick Banting and Charles Best discovered insulin in 1921, they saw their research literally save lives. However, the burden associated with managing diabetes continued to prevent many patients from living life to its fullest. Ongoing research advances over the years have enabled kids like Patrick to pursue the same activities as their peers without a constant, looming fear of swings in blood sugar. "Technology has allowed me to prevent lows because it can predict when I will be going low. I can see trends that help me with decision making – what to eat, when to correct and so on," Patrick stated. "I hope technology in the future will be completely hands off and will make blood glucose corrections without my input."

The mission of the American Diabetes Association is to prevent and cure diabetes and to improve the lives of all people affected by diabetes. Since 1952, the ADA has supported scientists and the life-saving research they conduct to ensure people with diabetes, like Patrick, can live life to the fullest.

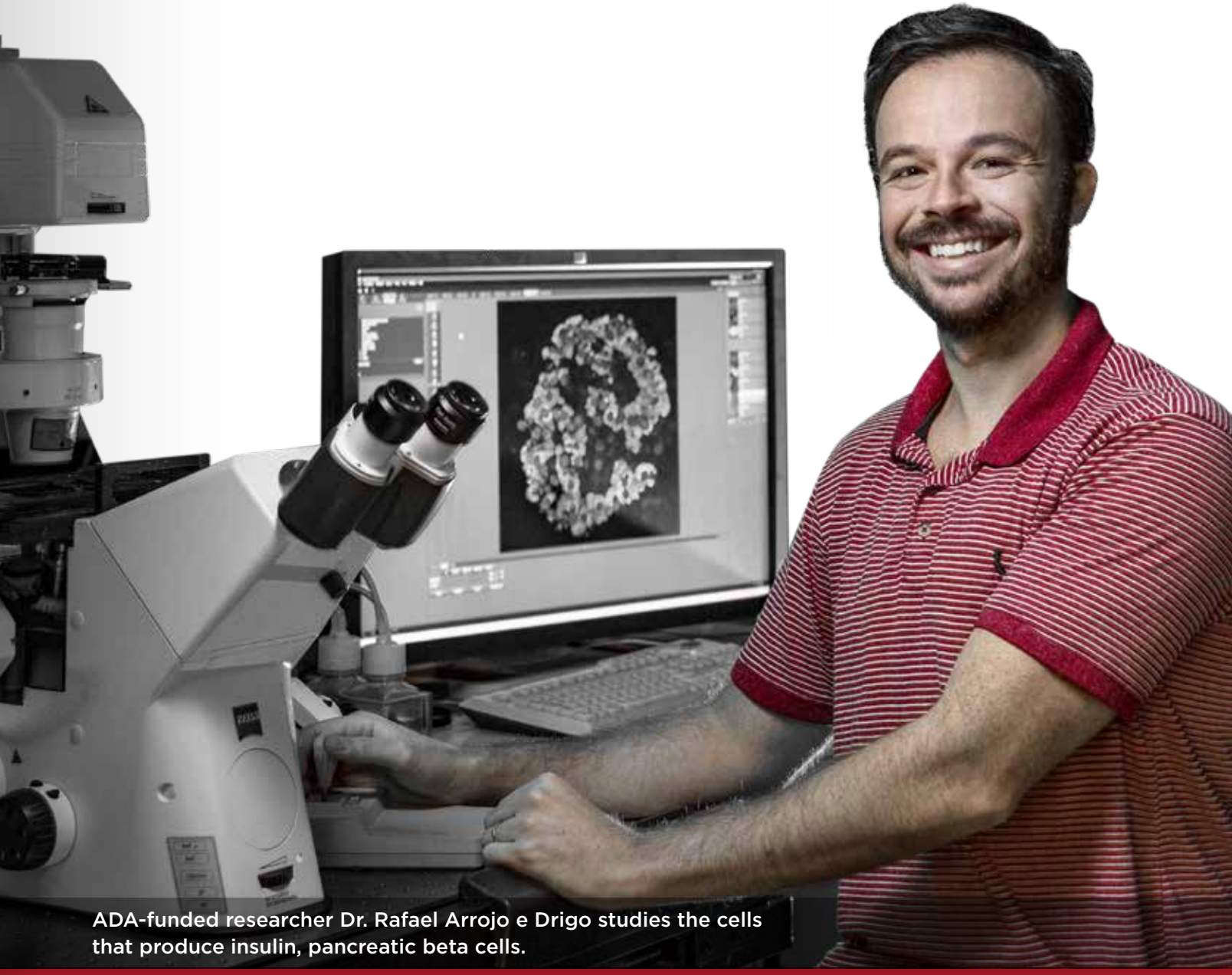
Patrick Swingle and his Father, Joe Swingle, attend the ADA's 78th Anniversary celebration.

TYPE 1 DIABETES:

T1D is an autoimmune disease characterized by destruction of insulin-producing cells in the pancreas.

On October 30th, 1920 a young physician sat at his desk preparing a lecture on the pancreas for medical students. While thumbing through the latest research publications on this mysterious organ, he came across one that piqued his interest. With a few strokes of his pen, he jotted down an experiment that would change the course of history. Dr. Frederick Banting had just set in motion the discovery of insulin.

Today, the ADA supports scientists committed to improving the lives of people with T1D through innovative research. With scientists dedicated to solving the mysteries of this disease, finger pricks and insulin injections may soon be a thing of the past.



ADA-funded researcher Dr. Rafael Arrojo e Drigo studies the cells that produce insulin, pancreatic beta cells.

Communicating real time glucose levels to parents

Witnessing your child come of age can be both rewarding and distressing. Add in T1D, including the necessity for a transition from parent-care to self-care, and this life stage becomes even more complicated, often accompanied by reduced adherence to treatment regimens and increased risk for poor health outcomes. **Bree Holtz, PhD,** of Michigan State University, received an **ADA Innovative Clinical or Translational Science award** to address this issue. Dr. Holtz created an application called MyT1DHero which links real time patient health data to a parent or caregiver mobile device, thus facilitating a more stable transition period. Dr. Holtz demonstrated that parents were pleased with the design and functionality of the app. Remarked one parent, "I really did like receiving the blood sugars, I always thought I was more aware of what was going on than I really was, so that was an eye opener."

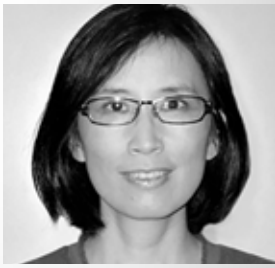
What's next? Dr. Holtz now wants to test whether using the app improves health outcomes in adolescents transitioning to self-care. A pilot study is underway.

Preventing T1D with an innovative therapy

Using a combination of genetic and blood tests, doctors can now accurately predict people at high risk for developing T1D. However, there is still no way to prevent T1D from occurring. **Kenneth Brayman, MD, PhD,** of the University of Virginia, was granted an **ADA Innovative Basic Science award** to change this. He has identified a factor, called IgM, that doesn't work properly in people with T1D and causes immune cell dysfunction, leading the immune system to attack the body's insulin-producing cells. Dr. Brayman demonstrated that IgM obtained from healthy human donors prevented progression of T1D in mice. This was not the case when the IgM was obtained from subjects that already had diabetes.

What does this mean? Dr. Brayman has recently filed a patent application and hopes to advance clinical testing that might make IgM therapy a reality for people at high risk for T1D.

Improving transplantation to eliminate the need for insulin injections



For people with T1D, finger pricks and insulin injections are a part of everyday life. Can research change that? **Qizhi Tang, PhD,** of the University of California San Francisco, received an **ADA Innovative Basic Science award** supported by the Foundation for Diabetes Research to investigate how to make insulin independence through transplantation a possibility for all people with T1D. Dr. Tang and her team of researchers are working to figure out how to transform stem cells into insulin-producing cells and how to ensure they survive following transplantation. They recently published a study highlighting several simple ways to make sure these cells remain functional after transplantation.

So what? The ability to convert stem cells into insulin-producing cells means the possibility of a limitless supply of cells to transplant. With this approach, it may become possible for all people with T1D to eliminate the need to administer insulin.

TYPE 2 DIABETES:

T2D occurs when environmental, genetic and socioeconomic factors conspire to reduce insulin production and utilization.

In 1996, Dr. John Eng stood next to his poster in the exhibit halls of the ADA's 56th Scientific Sessions in San Francisco, California. For years, Dr. Eng had been researching a molecule he first identified from the saliva of the Gila monster, a species of venomous lizard native to the Southwest of the United States. This molecule seemed to enhance the secretion of insulin and improve glucose control in animal models of diabetes. A leader from a small biotech company read Dr. Eng's poster and set up a meeting to discuss furthering development of this molecule. A few years later, the diabetes medication Exenatide was approved to treat patients with T2D.

Today, the ADA invests in all aspects of research focused on T2D, spanning laboratory to clinical work and everything in between. What ties the research together, no matter the stage of development, is a focus on improving the lives of people with T2D and ultimately curing this disease.

A poster author presents her findings during a moderated poster tour at ADA's 78th Scientific Sessions in Orlando, FL.

Determining the genetic risk for gestational diabetes

More than 100 genetic variants have been linked to risk for developing T2D in humans. However, the extent to which these same genetic variants might affect a woman's probability of getting gestational diabetes has not been investigated. **Pathway to Stop Diabetes® Accelerator awardee Marie-France Hivert, MD,** of Harvard Medical School, set out to answer this critical question. Dr. Hivert found that indeed genetic determinants of T2D outside of pregnancy are also strong risk factors for gestational diabetes. This study was published in the journal *Diabetes*.

The implications? Because of this finding, doctors in the clinic may soon be able to identify women at risk for getting gestational diabetes and take proactive steps to prevent it.

Incentivizing behavior changes in youth at risk for developing diabetes

Incidence of T2D is rapidly increasing in America's youth. Unfortunately, children often do not have the ability to understand how everyday choices impact their health. **Davene Wright, PhD,** of Seattle Children's Hospital, was granted an **Innovative Clinical or Translational Science award** to determine whether using incentives, directed by parents, can improve behaviors related to diabetes risk. In a study published this year she outlined what incentives were most desirable and feasible to implement. A key finding was that incentives should be tied to behavior changes and not to changes in body-weight.

What's next? With this information Dr. Wright now wants to see if incentives do indeed change a child's eating habits and risk for developing T2D.

Understanding the relationship between fructose and T2D

Soda consumption is associated with increased risk of developing T2D. But do we know precisely why? **Innovative Basic Science awardee Cholsoon Jang, PhD,** of Princeton University, wanted to answer this important question. In a study that received significant media attention, Dr. Jang determined that, in low amounts, fructose is metabolized in the intestines and never makes it into circulation. However, in high doses, like those found in soda, fructose overwhelms the normal intestinal disposal route and enters the bloodstream, ultimately causing toxicity in the liver and increasing risk for T2D.

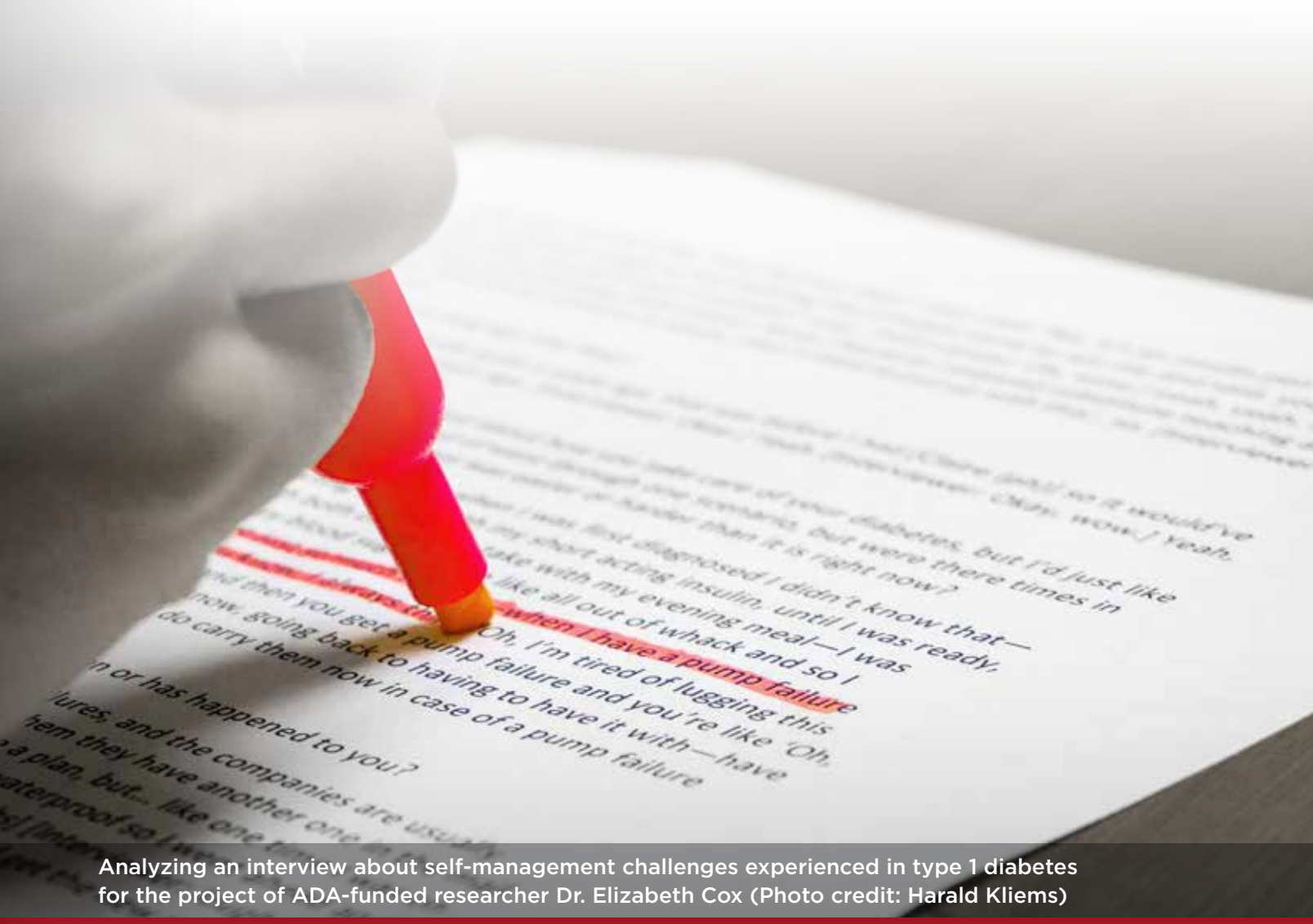
Where do we go from here? These findings suggest a mechanism by which soda consumption influences T2D risk and supports nutritional guidance to reduce soda consumption in people with or at risk for T2D.

DIABETES COMPLICATIONS

Both T1D and T2D can cause serious complications including heart disease, amputations, blindness and kidney disease.

In 1993, a study in the *New England Journal of Medicine* showed that better glucose control reduces complications related to T1D. A similar study was published in 1998 for T2D. With this in mind, scientists set out to develop new medications to improve glucose control. Today, we have 12 classes of medications approved to improve glucose control for people with diabetes and technological solutions like the insulin pump and continuous glucose monitoring have been made widely available for people with diabetes. To come full circle, in 2014 we learned that rates of serious diabetes complications including heart attacks, stroke, amputations and kidney disease all declined significantly during the previous 20 years.

Today, thanks to research, people with diabetes are living longer, healthier lives. The ADA is dedicated to continuing to improve the lives of people with diabetes by supporting research that ensures continued decline of diabetes complications.



Analyzing an interview about self-management challenges experienced in type 1 diabetes for the project of ADA-funded researcher Dr. Elizabeth Cox (Photo credit: Harald Kliems)

Preventing heart disease while maintaining glucose control in T2D

People with T2D are at significantly increased risk for developing heart disease. While increasing insulin levels is important for managing diabetes, too much insulin may contribute to atherosclerosis by stimulating processes unrelated to glucose lowering. **Jenny Kanter, PhD,** of the University of Washington, wanted to resolve this insulin catch-22. In 2016, Dr. Kanter received an **ADA Innovative Basic Science award** supported by the Amaranth Diabetes Foundation. This year, Dr. Kanter published a fascinating study demonstrating that an insulin-like molecule can exhibit insulin's glucose lowering effects without activating the processes that promote heart disease.

What does this mean? Further progression of this novel therapy could lead to a treatment for diabetes that also prevents heart disease.

A novel therapy for treating foot ulcers in diabetes

Diabetes is the leading cause of non-traumatic lower-limb amputations in the U.S. An impaired ability to sense and heal wounds is a major contributor to this diabetes complication. **Mayland Chang, PhD,** of the University of Notre Dame, was granted a **Pathway to Stop Diabetes® Visionary award** to figure out a way to improve wound healing in people with diabetes. This year, Dr. Chang reported that she had identified a molecule that is higher in people with diabetes and which prevents effective healing of foot ulcers. Inhibiting this molecule with a novel drug significantly improved the ability to heal wounds in mice with diabetes.

Now what? Continued development of this compound could lead to a new therapeutic option to treat wounds related to diabetes.

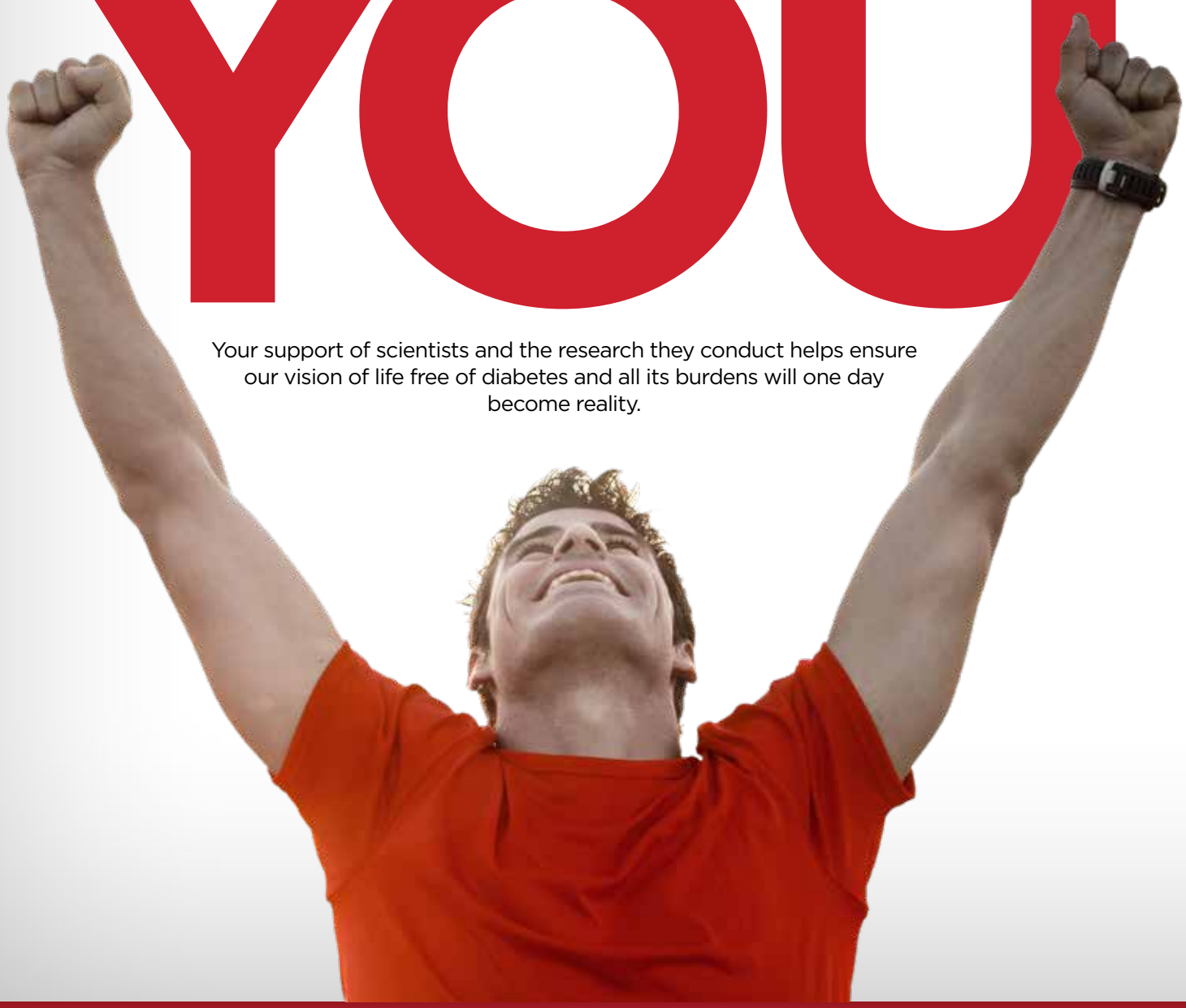
Identification of a new player in chronic kidney disease

Diabetes is the most common cause of chronic kidney disease, the serious condition in which kidney function progressively deteriorates, ultimately resulting in failure. Current therapies are non-specific and only slow the progression of this debilitating disease. To address this critical gap, the ADA secured financial support from Boehringer Ingelheim to fund the **Chronic Kidney Disease and Renal Insufficiency in the Setting of Diabetes Research Award. Janos Peti-Peterdi, MD, PhD,** of the University of Southern California, received one of these awards to study a peculiar group of cells in the kidney called macula densa cells. Using novel microscopy and imaging techniques, Dr. Peti-Peterdi discovered that in diabetes, macula densa cells secrete factors which impair the function of the kidneys.

What's next? Dr. Peti-Peterdi hopes to target these cells with a drug to halt progression of chronic kidney disease. To this end, he has filed a patent on this work this year.

DEAR PAST, PRESENT & FUTURE ADA DONORS, THANK YOU

Your support of scientists and the research they conduct helps ensure our vision of life free of diabetes and all its burdens will one day become reality.



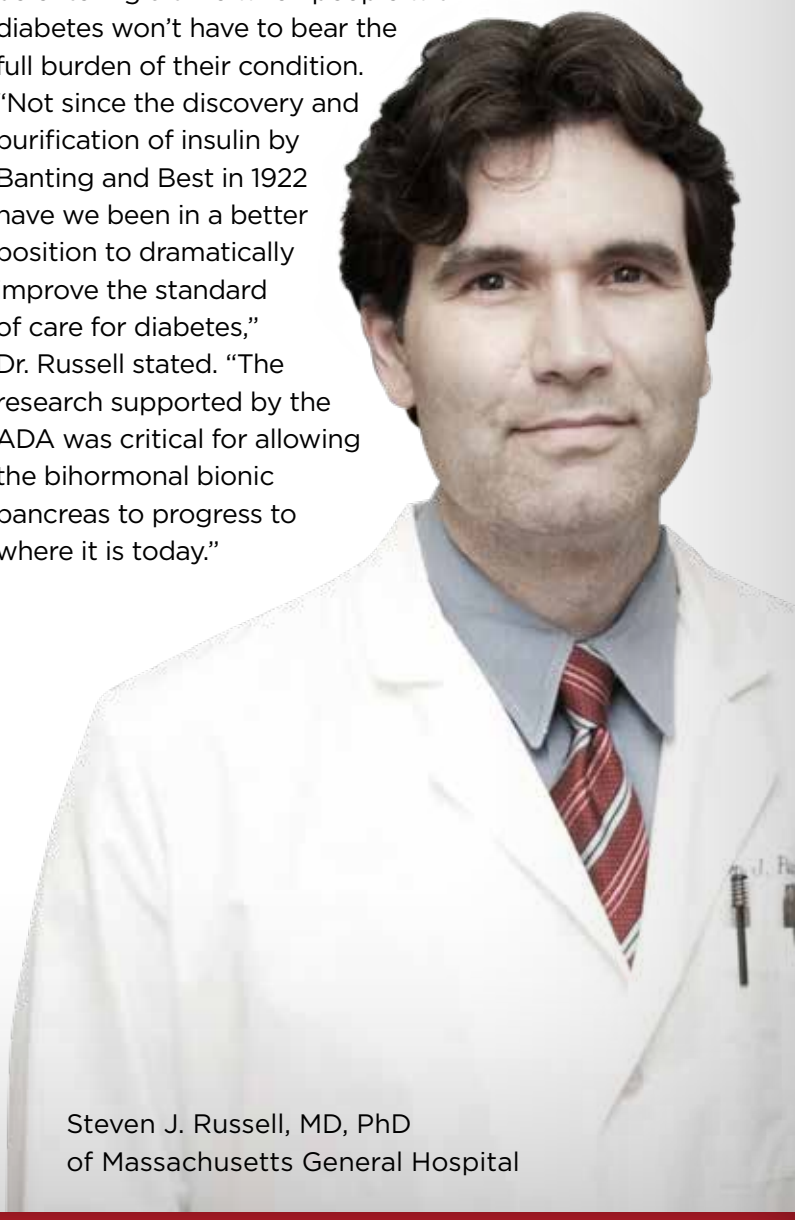
COMMITTED TO RESEARCH:
Breakthroughs For_Life

For people with diabetes, managing blood glucose is often a daily roller-coaster of highs and lows. With so many factors influencing glucose control, it can be challenging for even the most diligent people to keep within a target range. High glucose can be managed with insulin, however, even a slight miscalculation of dosage can result in low blood glucose, a condition called hypoglycemia, which is an acutely dangerous situation. This delicate balancing act is a major physical and emotional burden for people with diabetes and their loved ones. Unfortunately, no therapy currently exists that proactively prevents hypoglycemia.

In 2012 the American Diabetes Association funded Dr. Steven Russell, who proposed an innovative way to address the issue of hypoglycemia. Dr. Russell thought, what if we repurpose insulin pumps to administer the body's natural hormone glucagon, which quickly counteracts insulin to increase blood glucose during hypoglycemia? By coupling this 'glucagon pump' to a continuous glucose monitor, Dr. Russell believed he could proactively prevent hypoglycemia and the dangerous complications that come with it.

With his American Diabetes Association award, Dr. Russell was able to conduct a clinical trial to definitively test his idea. The results speak for themselves. Patients who used the automated glucagon pump saw a dramatic reduction in hypoglycemic incidents and significantly increased the time they spent within their ideal glucose range. Importantly, glucagon was well tolerated with no documented adverse reactions. Dr. Russell stated that "the outcome of this trial was critical in placing automated glucagon microdosing at the forefront in the fight against hypoglycemia."

Fast-forward six years and Dr. Russell and his collaborator, Dr. Ed Damiano, leveraged these results to generate the first bi-hormonal bionic pancreas. This device is capable of continuously monitoring glucose levels and automatically releasing an appropriate amount of insulin or glucagon to keep patients within an optimal range. The device, called the iLet, is the main product being developed by Beta Bionics, a company founded by Dr. Damiano. With the generation 4 iLet now entering pivotal clinical trials, we may finally be entering a time when people with diabetes won't have to bear the full burden of their condition. "Not since the discovery and purification of insulin by Banting and Best in 1922 have we been in a better position to dramatically improve the standard of care for diabetes," Dr. Russell stated. "The research supported by the ADA was critical for allowing the bihormonal bionic pancreas to progress to where it is today."



Steven J. Russell, MD, PhD
of Massachusetts General Hospital

IN THEIR OWN WORDS: ADA-funded researchers

Dr. Nicole Glaser: "Our group conducted the first randomized clinical trial of fluid therapies for children with diabetic ketoacidosis, a serious condition in T1D caused by insufficient levels of insulin. The results were published in the *New England Journal of Medicine* and will be instrumental in guiding treatment for children with diabetic ketoacidosis. Funding from ADA allowed us to gather substantial preliminary data to support this clinical trial. Without this funding, the trial would never have been possible."

Dr. Michelle Kimple: "In 2018, I was promoted to Associate Professor with Tenure at the University of Wisconsin-Madison School of Medicine and Public Health. My Innovative Basic Science award funding from the ADA and the productive research it supported, along with an ADA Minority Undergraduate Internship supplement, no doubt contributed to my successful promotion based on excellence in research and significant accomplishment in teaching."

Dr. Alexander Staruschenko: "The ADA has continuously supported my research and career; my projects on type 1 and 2 diabetes simply would not be possible without ADA funding. ADA gave me financial security and freedom to perform diabetes related research, which was a new area in my research portfolio. My ADA grant was a great push to pursue new research ideas, and an inspiration to eventually have the findings of my laboratory translated into the clinic."

THE NUMBERS TELL THE STORY

$834.4M
invested in research since **1952**

297
funded scientists at
104
institutions across
the United States in 2018

318
research projects
supported in 2018

133
in-training or early career
investigators supported in 2018

53
underrepresented minority
scientists funded in 2018

THE CASE FOR RESEARCH

"Through research funding, the ADA is not only advancing key targeted discoveries but also investing today in tomorrow's diabetes experts. I am optimistic that bringing and retaining these talented scientists in diabetes research will contribute to finally conquering the disease."

Jose C. Florez, MD, PhD
Massachusetts General Hospital
Harvard Medical School
Chair of ADA Research Policy Committee

RESEARCH MATTERS FOR_LIFE:

"The Prince Hall Shriners are pleased to be long-time supporters of the American Diabetes Association Research Foundation. Diabetes takes a disproportionate toll on African Americans and raising funds to support research is an important way that we can fight this costly epidemic. In fact, we have made a new $1M commitment—part of which will support new discoveries to better the lives of people with diabetes. We hope others will join us."

–Rev. Charles W. Davenport, 43rd Imperial Potentate, A.E.A.O.N.M.S., Inc.

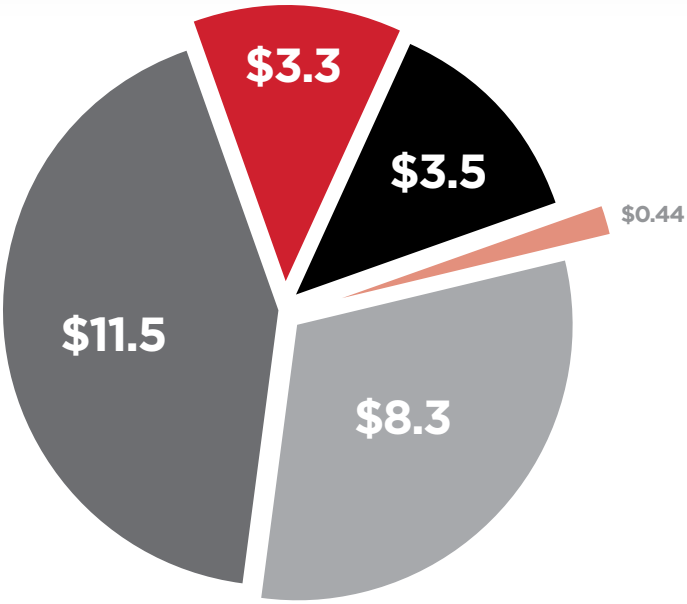
Every year, the ADA receives hundreds of promising grant proposals from talented investigators all over the country. We don't want to miss out on the next diabetes breakthrough. Help us to explore every single one.

By supporting research, you are giving life to people with diabetes and hope that we will one day find a cure.

Donate at **diabetes.org/supportresearch** or call **1-888-700-7029**

100% of donations made to the ADA Research Foundation support scientific investigations in the Research Programs project portfolio.

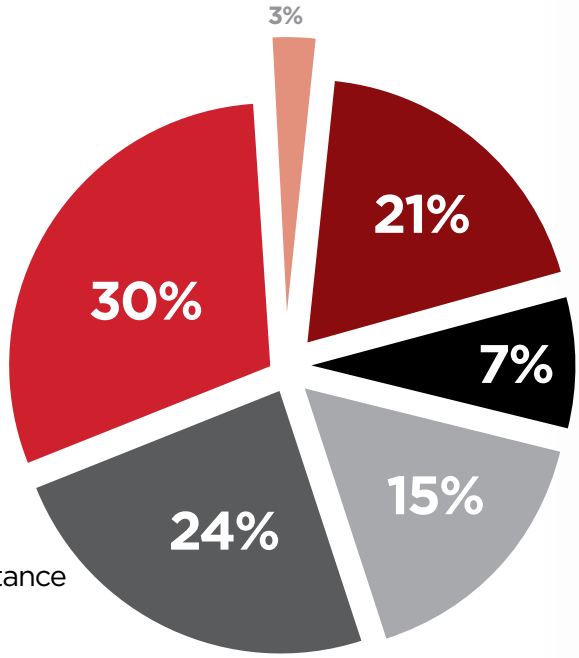
2018 RESEARCH FUNDING



Grant Type

Dollars in Millions

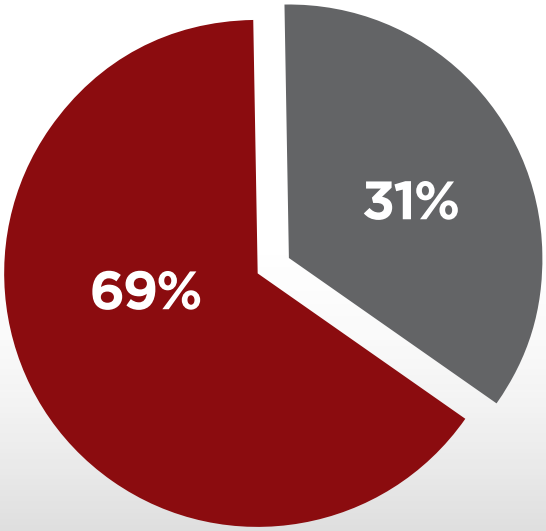
- Core Research
- Core Development
- Core Training
- Collaborative Targeted
- Pathway to Stop Diabetes



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

"We support diabetes research because we have family and friends who live with this disease every day. Because of new developments in ADA-funded research, these loved ones are living more productive lives. It is powerful to be a part of helping people with diabetes live longer, healthier lives. We encourage others to join us in imagining what brilliant ideas will be transformed into lifesaving discoveries next."

–Anonymous philanthropic supporter

American Diabetes Association. | Research Foundation

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Cover: Janice M. Huss, Ph.D. studying the estrogen-related receptor alpha which mediates skeletal muscle genetic and metabolic response to exercise.