Careers, Ideas, Progress HING.

American Diabetes Association. RESEARCH **PROGRAMS**

2014 YEAR IN REVIEW

A Message from Tamara Darsow, PhD Vice President, Research Programs, American Diabetes Association

In the face of the growing burden of diabetes, a disease that now affects 1 in 11 Americans, critical funding for the research necessary to improve health outcomes is shrinking. Federal research funding for diabetes from the National Institutes of Health amounts to just \$34.60 per person affected by diabetes. This level of funding is grossly inadequate for the scope of the problem and threatens the research progress already made to reduce complications and improve quality of life for people with diabetes.

Furthermore, bright young scientists are increasingly choosing other careers, including better-funded research areas and non-research positions.

The American Diabetes Association recognizes these issues as serious roadblocks to continued scientific progress and advances in diabetes care. Since 1952 the Association has committed to independently funding essential diabetes research. Our commitment is needed now more than ever.

With generous contributions from philanthropic supporters and corporate sponsors, the American Diabetes Association is dedicated to launching success stories by investing in early career scientists and innovative ideas that may provide the next breakthroughs in diabetes care. We're reflecting back and planning ahead. We're launching careers, launching ideas, launching progress.

Please join us.



A scientific career is a difficult endeavor. Often a decade or more of post-graduate training is required. The hours are long, the compensation is modest, and the progress is slow. With few academic positions available each year, the competition is stiff. Further complicating matters is a federal research budget that has been flat for 15 years. For scientists early in their careers without an established track record, it is difficult to compete for federal funding. One might ask with all these considerable challenges why people pursue scientific careers in diabetes research. It is because they are driven to discover and to help people with diabetes live better lives. The American Diabetes Association is committed to investing in these dedicated, bright emerging scientists—not just their projects. We know that without a strong, promising pipeline of researchers to make tomorrow's diabetes research advances, we will never meet our goal to Stop Diabetes®. Ninetyeight percent of the investigators we support remain in diabetes research. We are launching careers.

Measures of Success

Comparing researchers awarded Association Career Development Awards in 2005 to those not funded, the funded researchers:

- have been 21% more likely to receive subsequent NIH funding;
- have been 26% more likely to continue diabetes research; and
- have published 33% more scientific papers

Tamir Gonen, PhD, Howard Hughes Medical Institute's Janelia Research Campus

Dr. Tamir Gonen was awarded a Career Development grant in 2009. The funding was critical, allowing

him to continue the work that culminated in this year's high-profile publication describing the molecular structure of a protein responsible for shuttling glucose from the blood into cells. Based on these studies, we now understand in detail how glucose is attracted to and transported across the cell membrane so that it can be used or stored as an energy source. With this information, drug developers can begin targeting this protein for the design of new drugs capable of speeding up or slowing down the movement of glucose from blood to cells.

Dr. Gonen described the prospect of continuing this project as dire when he applied for Association funding in 2009, then based at the University of Washington. His lab was fairly new and he had spent most of his initial funding. Federal research funding was decreasing and becoming more difficult to secure.

Fortunately for Dr. Gonen and this important line of work, he was selected for an Association Career Development award. With the essential funding in hand, he was able to focus on science, rather than on searching for funding.



"The American Diabetes Association grant shielded us from the world. It helped us carry forward with the research at a time when federal funding was going down. The NIH doesn't have enough money and it is very difficult for people to raise enough funds to do research."

The Association grant preceded additional funding that has continued to sustain Dr. Gonen's research program. He was selected for a prestigious Howard Hughes Medical Institute (HHMI) Early Career Scientist Award, which led to his current position as a research group leader at HHMI's Janelia Research Campus in Ashburn, Virginia. Dr. Gonen credits his continued efforts in diabetes-related research to the Association's investment at a crucial time.

Stephen C.J. Parker, PhD, University of Michigan

Dr. Stephen Parker was selected for a *Pathway to Stop Diabetes* Initiator Award in January 2014—one of five scientists selected for *Pathway* awards in the program's inaugural class. Within months of earning the award, Dr. Parker found himself interviewing at top institutions across the country for his first faculty position. In fact, he had seven different interviews and received a job offer from each. He credits the *Pathway* award for his success in faculty interviews, noting that it demonstrated to prospective employers that he had already been vetted.

With no shortage of excellent choices, Dr. Parker accepted an offer as Assistant Professor in the Department of Computational Medicine and Bioinformatics at the University of Michigan, where his independent research career is launching.

In addition to being grateful for the funding, he also is taking full advantage of the mentorship and network that *Pathway* provides.



"I am immensely grateful, especially in this funding climate—not only for the substantial *Pathway* funding, but also for the access to mentorship and resources that being part of this community brings."

He has established productive relationships with members of *Pathway's* Mentor Advisory Group. Through collaboration with Mentor Advisory Group member Chris Newgard, PhD, at Duke University, Dr. Parker is beginning to study rat islets, which provide a better model to humans than the mouse cell lines he had previously planned on using. This work will help Dr. Parker validate his comparative genomics approaches, and also translate human genomic information to model systems.



"The greatest challenges I have faced have been getting to the point of securing the first level of funding as an independent investigator. That's why the American Diabetes Association support has been so critical to my career."

Janet Snell-Bergeon, PhD, MPH, University of Colorado Denver

As a doctoral student, Dr. Snell-Bergeon was involved in a large study examining cardiovascular disease risk in women. When she examined the results, she discovered common risk factors for women with type 1 diabetes and those with other endocrine disorders she had been studying. These results first got her interested in investigating cardiovascular complications of diabetes.

Women with type 1 diabetes lose the cardiovascular protection typically seen during the premenopausal years. Dr. Snell-Bergeon has found that insulin resistance, a characteristic historically associated with type 2 diabetes, is significant in young women with type 1 diabetes and she believes this insulin resistance is key to the increased cardiovascular risk present in type 1 diabetes. She aims to determine how.

Dr. Snell-Bergeon's early career has been supported through a series of grants from the American Diabetes Association, starting with a Mentor-Based Fellowship in the laboratory of Marian Rewers, MD, PhD. Her success as a fellow led the University of Colorado Denver to offer her a faculty position in 2008. In 2010, Dr. Snell-Bergeon was awarded a Junior Faculty Award from the Association. In 2014, she earned an Association Career Development Award and was promoted to Associate Professor. With the support of the Association awards, Dr. Snell-Bergeon has been able to successfully move her research in an independent direction and obtain funding from the NIH. Her career path perfectly illustrates how the Association's research funding prepares young investigators for successful careers in diabetes research.

Thank You to Our Philanthropic Supporters

Innovative ideas and persevering passion can only launch progress if first ignited by the opportunity to succeed. Without generous gifts from dedicated individuals, corporations, family foundations and other organizations, many pivotal research initiatives would never leave the launching pad.

As demonstrated throughout the pages of this report, the research supported by the American Diabetes Association contributes immeasurably to medical advances that allow people with diabetes to live longer, healthier, and more comfortable lives. It is with deep honor and appreciation that we thank everyone who made contributions to support the American Diabetes Association's Research Programs in 2014.

With a mission to fund innovative science and a focus on projects that are early in development, the American Diabetes Association is on the forefront, fostering tomorrow's advances in prevention, care and eventual cures in diabetes. Our investments are paying off. Eightyseven percent of Association-supported investigators successfully obtain subsequent federal funding to continue their investigations. **We are launching ideas.**



Return on Investment

Every \$1 the American Diabetes Association invests in diabetes research yields \$4 of federal funding to take innovative discoveries to the next step.



Can a breath test detect diabetes risk?

Ruchi Mathur, MD at UCLA is testing the methane produced by certain bacteria in patients' breath. She's already correlated this test to BMI. Now she's testing whether antibiotics can improve metabolic function in people with high levels of methaneproducing bacteria.

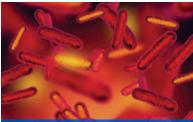
Dissecting the Host-Microbiome Relationship in Diabetes

Emerging science suggests that the microbiome—the bacteria that live in our gut and on our skin—plays a critical role in human health. Many factors, including diet and medication, can change the composition of the microbiome, and differences in the composition can subsequently change inflammation and metabolic function, leading to risk for diabetes and obesity.

Studies have already shown links between particular microbiome compositions and type 1 diabetes, as well as obesity and type 2 diabetes.

More research is required to determine how these unique microbiome compositions affect individuals' metabolic and immune states.

In addition to our core program grants that are funding investigator-initiated research in this area, the Association has also funded a series of targeted research projects on the microbiome with support from GlaxoSmithKline. In total,



Targeted grants with support from GlaxoSmithKline are helping scientists uncover the surprising links between microorganisms and diabetes.

our current portfolio includes 17 grants examining the gut and gut hormones and five specifically examining the role of the microbiome in diabetes.

Diabetes and the Microbiome Research Symposium

In October 2014, the Association partnered with JDRF to convene a research symposium featuring both abstract submissions and invited speakers discussing the state of the art in microbiome research in diabetes. Conference proceedings will be published from this event, detailing what is known and what questions



remain unanswered about the connections between the microbiome and metabolic and immune systems. Importantly, the proceedings will also feature recommendations for additional research needed to accelerate progress in this innovative and promising area of science.

Bringing the Artificial Pancreas Closer to Reality

Type 1 diabetes is often diagnosed in childhood and results in a lifelong dependency on insulin therapy. Adherence to glucose monitoring, insulin administration, diet and physical activity regimens can be overwhelming. Research efforts have already brought continuous glucose monitoring (CGM) and insulin pump technologies to patients. But, advances that further reduce the everyday burdens of diabetes management are still needed. To this end, the Association is funding research into new technologies capable of automatically responding to high or low glucose levels with infusion of insulin—a so-called "artificial pancreas".

A significant hurdle to regulatory approval of automated artificial pancreas technology has been the lack of a mechanism to avoid the dangers of low blood glucose (hypoglycemia). As diabetes management improves, and more patients are able to tightly

regulate blood glucose levels, incidence of hypoglycemia as a result of diabetes therapy is increasing. In 2011, emergency room visits for hypoglycemia (282,000) outnumbered visits for high blood glucose

(hyperglycemia; 175,000 visits). With support from Novo Nordisk Inc., the American Diabetes Association is funding a series of grants to develop ways to prevent hypoglycemia.

In addition, Association-funded researchers like Shuiqin Zhou, PhD at the College of Staten Island and Zhen Gu, PhD at North Carolina State University are developing all new materials, including implantable or injectable gels that can sense glucose levels and respond with the appropriate release of insulin.

Re-examining Drugs and Drug Targets for New Diabetes Therapies

Sometimes the best progress in science comes from re-examining what we thought we knew. This idea drives one component of the *Pathway* program that seeks to bring scientists from different fields to diabetes research. They will have different tools and new ways of thinking about the hurdles to the next big advances in diabetes.

In the first class of *Pathway* scientists, one awardee was selected in the "new to diabetes research" category. Wolfgang Peti, PhD is a structural biologist at Brown University who has studied neurodegenerative diseases in the past. Now, he is applying his expertise to learn more about the molecules that regulate blood glucose. Using sophisticated tools, he is looking for new ways to develop diabetes drugs that will act on molecules that may have been overlooked or abandoned previously.

The Association is also supporting projects that are taking second looks at drugs that are already approved for other diseases. Scientists

are using what they've learned about what goes wrong in diabetes and re-examining the function of existing medications to determine whether they could also help people with diabetes. A major advantage to this approach is that, if successful, such medications could reach patients faster since they have already passed the rigors of clinical trials in humans and have met with regulatory approval.



Can two hormone pumps replace the function of a pancreas?

Steven Russell, MD, PhD at Massachusetts General Hospital has developed a glucagon pump and linked it to CGM and insulin pump technology to create a "bionic pancreas."



Targeted grants with support from Novo Nordisk Inc. are helping scientists develop new ways to prevent hypoglycemia.



Can an Alzheimer's drug treat diabetes?

With the support of a first-time donation of \$50,000 from the Kahlert Foundation, Inc., Xiao-Jian Sun, PhD at the University of Maryland, Baltimore is looking for ways to re-purpose existing drugs to treat diabetes.

Treating diabetes looks much different today from how it looked more than 60 years ago when the American Diabetes Association funded its first research grant. Thanks to investments in research, there are more tools. medications and information available for treatment and prevention of diabetes. These advances have made a tremendous impact. People with diabetes are living longer, healthier lives. Dramatic reductions in diabetes complications have been realized. But our work is not done. Despite these improvements for individuals, the number of people with diabetes continues to grow. It is estimated that by 2050, one in three people could have diabetes. We need to accelerate our efforts to efficiently bring advances in prevention and care to all people with diabetes. With our investments in clinical and translational research, we are working to end the burden of diabetes. We are launching progress.

Reductions in Complications

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Since 1990, research advances have led to:

- ▼ 52.9% reduction in STROKE
- 67.8% reduction in HEART ATTACK
- ▼ 51.4% reduction in **AMPUTATION**

28.3% reduction in END STAGE RENAL DISEASE

64.4% reduction in HYPERGLYCEMIC CRISIS DEATHS

Disparately Impacted Populations

Diabetes and its complications disproportionately affect minorities, older adults, and individuals with co-morbid conditions. These populations may face particular factors that require specialized approaches to addressing diabetes management and complications.

The American Diabetes Association is currently funding 18 active research grants in health disparities related to diabetes.

Understanding distinct needs of special populations will lead to better care and health outcomes. Behavioral interventions and patient education, as well as particular therapies that may work differently in various populations, should be tailored to individuals



Targeted grants with support from Lilly are examining diabetes care in older adults – the population at highest risk with more than 1 in 4 people over the age of 65 affected.

based on research dedicated to distinguishing needs and barriers to effective treatment strategies. It is becoming increasingly clear that there is no "one size fits all" approach to managing diabetes.



What special care needs do older minorities with diabetes have? Ana Quinones, PhD at Oregon Health & Science University is studying behavioral interventions to find the most effective therapies for different populations.

Diabetes and Pregnancy

Several recent studies suggest that the environment in the womb has long term effects on the offspring's health. Factors such as mother's diet, exposure to chemicals and glycemic control can affect the health of the child throughout its life, regardless of the child's genetic makeup.

The Association is currently funding 10 active research grants in diabetes and pregnancy, including gestational diabetes and maternal programming of offspring's health.

Research in animal models has shown direct relationships between mother's diet and glucose levels on the offspring's metabolic health. New clinical studies are looking at children of women who had diabetes or were exposed to environmental toxins, such as air pollution, during pregnancy. This information can help inform the development of new guidelines for healthy pregnancy and help to identify the children at highest risk for developing diabetes so that early interventions can be made with the hope of preventing it.



How does the womb impact your health? Pathway scientist Kathleen Page, MD at the University of Southern California is looking at whether gestational diabetes leads to changes in children's brain development that are linked to diabetes and obesity.



How can 29.1 million people get effective diabetes care?

Salim Virani, MD, PhD at Baylor College of Medicine is studying patients with diabetes in the Veteran's Affairs healthcare system to determine whether the same care is provided with similar outcomes when patients visit physicians versus nonphysician health care providers.

Primary Care of Diabetes

With the rising prevalence of diabetes and the expansion of insured Americans, an increased demand for diabetes care is imminent. There are shortages among both endocrinologists and primary care physicians, and more research is required to determine the safety and efficacy of using alternative health care providers to manage diabetes.

The Association is currently funding seven active research grants in health care delivery, examining such aspects of care as the use of technology to promote treatment and lifestyle adherence and

development of medication algorithms to better direct primary care management of diabetes.

The American Diabetes Association is the leader in providing evidence-based guidelines and standards of care to guide health care providers in diagnosis, treatment and management of people with diabetes. These tools are regularly reviewed and updated based on the latest research. Studies on



Targeted grants with support from Sanofi are helping researchers examine the best health services for clinical care of diabetes.

how to best manage care for the growing population of people with diabetes will inform these evidence-based clinical practice guidelines.



Where is personalized medicine for diabetes?

Alan Shuldiner, MD at the University of Maryland Medical Center has implemented a Personalized Diabetes Medicine Program to screen and diagnose monogenic forms of diabetes – rare types of diabetes caused by single gene mutations. Using genetic tests, appropriate therapies for these often misdiagnosed forms of diabetes can be prescribed.

Genetics and Diabetes

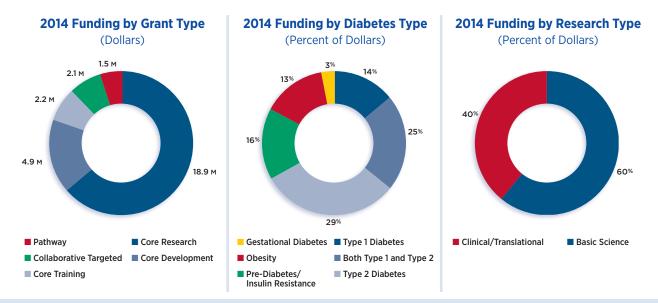
Diabetes is caused by various genetic and environmental factors. The multitude of causes makes discovery of a single cure for diabetes unlikely. The Association invests in a broad portfolio of research areas related to diabetes with the understanding that scientific breakthroughs often arise from unexpected places. Our breadth of research includes significant investments in projects investigating genetic contributors to diabetes.

The Association is currently funding 26 active research grants in genetics and diabetes. These grants range from examining ways to personalize treatment approaches to patients with specific genetic mutations, to seeking to identify people at greatest risk for developing type 1 diabetes. These studies are important to expanding the ability to apply early and appropriate treatment, and the results may even allow for at-risk individuals to be identified early enough to prescribe interventions that might prevent progression of diabetes.

American Diabetes Association Research Programs Investments

Since the American Diabetes Association launched its Research Programs in 1952, it has funded nearly 4,500 research projects, investing more than \$700 million in diabetes research.

In 2014 alone, the Association funded 376 new and continuing research grants and made nearly \$30 million in diabetes research funding available through its four major grant programs: the Core Research Program, the *Pathway to Stop Diabetes* Program, Research Co-Support, and Collaborative Targeted Research. These funds supported 364 investigators at 143 leading academic research institutions across the U.S.



One hundred percent of donations made to The American Diabetes Association Research Foundation will support scientific investigations in the Research Programs project portfolio. For more information about the Research Foundation please call **1-888-700-7029**.



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