This past year marked the American Diabetes Association’s 75th Anniversary. In honor of this important milestone, we took time in 2015 to reflect on the many advances realized through research that have helped people with diabetes live longer, healthier lives. The Association was founded in 1940, just 18 years after the first person with diabetes was treated with insulin. Twelve years later, in 1952, we began funding research grants. Since that time, we have invested more than $735 million in more than 4,500 research projects. Without a doubt, this investment has been essential to progress in diabetes care over the last 60 years and has dramatically improved health outcomes and the daily lives of people with diabetes.

When we funded our first research grant, treatment for diabetes was limited to insulin delivered with large needles through non-standardized syringes. Today, we know that tight blood glucose control reduces the complications of diabetes, and we have 12 different classes of medications and several formulations of insulin to achieve better blood glucose control with fewer side effects. We have insulin pumps and continuous glucose monitors that make everyday diabetes management more convenient and safer. We understand how nutrition and physical activity influence diabetes. We have more insight into how the environment and the neighborhoods in which we live impact diabetes risk and outcomes.

None of these advances and innovations would have been possible without research, the scientists who commit their lives to progress and discovery, and people like you whose vision and hope drives such generous support of the Association’s research mission.

The American Diabetes Association remains committed to ensuring that brilliant minds are attracted to diabetes research. We support innovative, early-stage research projects in all topics relevant to diabetes and diabetes-related conditions. This support allows researchers to explore untested ideas and learn important details that translate to new therapies and better clinical care. These scientists and their big ideas have shaped our history and hold the promise for an ever brighter future for people with diabetes.

In honor of the Association’s 75th anniversary, this year’s annual report highlights where we have been and where we are going in a few promising areas of diabetes research. We are proud of the progress that you have helped foster, and we are committed to pushing onward toward our shared vision—a life free of diabetes and all of its burdens.

Thank you for your support.

Tamara Darsow, PhD
Vice President, Research Programs
American Diabetes Association
W e encourage scientists to think outside the box and explore new ideas that can yield high rewards. History tells us that when it comes to scientific breakthroughs—such as the discovery of insulin—ingenuity and imagination are critically important. As we examine the progress researchers have made in several interesting topic areas, it is obvious that investments in innovative approaches have yielded significant advances.

**Regenerating and Replacing Beta Cells**

Insulin is a life-saving therapy. Yet frequently interrupting daily responsibilities and enjoyable moments to test blood glucose levels and inject another dose of insulin can be inconvenient and frustrating. And even under ideal conditions, injected insulin is not as safe and effective as natural insulin secreted from healthy beta cells. Diabetes researchers are working on developing ways to replenish or replace the insulin-producing beta cells in people with diabetes. The idea is that new, properly functioning beta cells could reverse or effectively cure diabetes.

One way to replace beta cells is through the transplantation of pancreatic islets. Though substantial progress has been made, transplants are not widely available to people with diabetes for several reasons. The number of tissue donors is very small and each transplant requires a large number of islets. Many pancreatic islets do not survive transplantation in the long term. And transplant recipients must undergo immunosuppressive therapy to avoid rejecting the donated tissue.

Many of the limitations of donor-derived islets can be addressed with stem cell technology. Stem cells have the remarkable potential to develop into many different cell types. Because type 1 diabetes is characterized by a loss of a specific cell type—the pancreatic beta cell—the disease is a top candidate for treatment or cure through stem cell therapy. Recent progress in stem cell differentiation suggests that an unlimited source of beta cells is likely to become available in the next several years.

Current research efforts are addressing how to use these new sources of cells, how to ensure that these cells live and function after transplantation, and how to best control immune responses against the transplanted tissue.

To prevent the immune system from rejecting transplanted beta cells, researchers are investigating ways to surround pancreatic islets in engineered materials that can block immune cells from detecting them as “foreign invaders.” This process of “encapsulation” is no small task. The encapsulating material must be porous enough to allow oxygen and vital nutrients to reach the islets and to allow insulin to be released from the islets into the bloodstream. Yet, it must be impenetrable to immune molecules.

Another approach is to find a way to use one’s own cells to generate new beta cells. Scientists have discovered ways to force cells from adults to return to an undifferentiated “stem cell” state where they hold the potential to become many different cell types. These cells can then be conditioned to create new beta cells that theoretically could be transplanted back into the same donor’s body, where they would be recognized as “self” and protected from the immune system. This would eliminate the need for immunosuppressive therapies following transplant. Scientists also have made significant progress in understanding how beta cells normally develop and reproduce. This information is fundamental to developing new therapies that might prevent beta cell destruction before diabetes develops or regenerate the body’s damaged beta cells. If the body can produce enough of its own functional beta cells, then transplant would not be necessary.

The American Diabetes Association invests in all of these approaches, which hold promise in overcoming the present barriers to effective islet transplantation.

**More than 80 percent of transplanted islets die within the first week after surgery. Qizhi Tang, PhD, is determining what conditions might help beta cells survive transplantation. With a grant co-sponsored by the Foundation for Diabetes Research, Dr. Tang is experimenting with mouse beta cells and beta cells derived from human stem cells. She found that low oxygen and nutrient deprivation led to cell death, but she is experimenting with ways to promote cell survival so that transplantation will become more effective.**

**Adolfo Garcia-Ocana, PhD, is studying whether a compound called dextran sulfate can prevent development of type 1 diabetes, by both protecting beta cells from cell death and encouraging new beta cell production. If successful, these laboratory-based studies, supported by a donation from the F.M. Kirby Foundation, will justify clinical studies into the use of dextran sulfate as a prevention or treatment strategy for people with type 1 diabetes.**

**Why I Support the American Diabetes Association**

"We are a family foundation, and type 1 diabetes has struck our loved ones; the work of Dr. Garcia-Ocana offers us hope by focusing on basic science that could prove critical to future developments to prevent, delay, or reverse type 1 diabetes. This work illustrates the high standard of research that we expect and that the American Diabetes Association delivers."

- Dillard Kirby, President & Director, F.M. Kirby Foundation
Using Technology to Mimic a Healthy Pancreas

Until diabetes can be effectively cured or put into remission through replacement of dysfunctional or destroyed beta cells with functional, responsive insulin-producing cells, the next best approach is taking the guesswork and the constant worry out of managing diabetes by using advanced devices and technologies.

The insulin pump became available in the late 1970s and over the decades has evolved to become smaller and more practical for everyday use. Still, insulin pumps have to be programmed and mealtime boluses given based on blood glucose readings. Historically this was done using finger-stick blood glucose monitoring, but more recently continuous glucose monitors (CGMs) have become more common.

CGMs were originally used for research starting in the mid-1970s. In the mid-1990s, CGMs became available for physicians to use to track trend data for their patients over a period of a few days. Only in the early 2000s did CGMs become approved for patient use. Yet, people who use CGMs still have to use traditional glucose meters to calibrate and verify the CGM readings and dose insulin.

While these technological advances make managing diabetes easier, the ultimate goal is to minimize the management burden by creating a so-called “artificial” or “bionic” pancreas that would link CGM directly to insulin pumps using a computer algorithm to automatically detect and respond to glucose fluctuations. However, development of such a system has been hampered because of limitations in current CGM technology and an inability to avoid potentially dangerous low blood glucose levels through existing technologies.

The American Diabetes Association is invested in overcoming these hurdles. To address the issues related to low blood glucose risk with insulin pump technology, several of our funded projects are examining the use of dual hormone technologies that incorporate glucagon—the hormone that counteracts insulin. When blood glucose levels fall below a certain level, then glucagon would be released to return blood glucose levels to the safe range, operating much like the healthy pancreas does.

Nanotechnology offers another frontier in potential diabetes management advances. By encouraging interdisciplinary collaboration and attracting new ideas to solve diabetes problems, the American Diabetes Association is supporting several projects that are using this molecular-scale engineering. In an exciting advance this year, an American Diabetes Association Pathway to Stop Diabetes scientist announced his development of an innovative “smart insulin” patch that takes a slightly different approach to the artificial pancreas. The patch imitates the body’s beta cells by both sensing blood glucose levels and responsively releasing insulin using a nanotechnology that leverages bioengineering, biochemistry, and materials science.

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Progress is not possible without people. The scientists whose brilliance, dedication, and passion lead them to pursue an often difficult career path are the driving force behind biomedical advances. We know that unless their diabetes research careers are supported, they will be forced to choose other fields, and advances in diabetes research will stall.

The American Diabetes Association is focused on attracting and retaining the best and brightest scientists to diabetes research. Our commitment is making a difference.

Ninety-nine percent of researchers who have received American Diabetes Association research funding report remaining in diabetes research five years after the conclusion of their grants. Their successes and their enduring dedication to answering the questions that lead to progress for people with diabetes are worth celebrating.

Today, thanks to decades of critical research, people with diabetes are living longer, healthier lives. They have better treatment options. Their diabetes research careers are supported, they will not be forced to choose other fields, and advances in diabetes research will stall.

The American Diabetes Association is committed to funding the research that promises tomorrow’s advances and, one day, a life free of diabetes and all its burdens.

The American Diabetes Association has invested more than $735 million in more than 4,500 research grants.

A sampling of 93 scientists whose grants ended between 2009-2011 showed:

- 92% secured subsequent diabetes research funding.
- An initial investment of $35.3 million led investigators to secure $260.2 million in subsequent funding. That’s $7.37 for every dollar invested by the Association!
- Since their grants were funded, these scientists have:
  - Been promoted in their careers (75% of those eligible for promotion).
  - Published their results in 491 papers (on average 5.3 per grant) in peer-reviewed scientific journals.
  - Been cited in 6,414 subsequent publications, significantly moving the field forward.
  - Delivered 1,197 scientific presentations (on average 12.9 per grant).
  - Remained dedicated to diabetes research (99%).

Government funding agencies such as the National Institutes of Health (NIH) often require significant data in grant applications to consider funding an idea. However, it can be difficult for scientists to conduct experiments to test a novel idea without the funding to support it.

That’s why the American Diabetes Association is invested in funding great ideas, even very early in development, that are put forth by promising researchers.

In 2005, the American Diabetes Association granted one of its Career Development Awards to Pere Puigserver, PhD, now at Dana-Farber Cancer Institute in Boston, to pursue a great idea. With this funding, Dr. Puigserver and his colleagues discovered new insights into how nutrients impact cellular signaling and the production of glucose in the liver. This work led to several seminal publications that have driven this field forward. The career development funding allowed Dr. Puigserver to establish a baseline of critical understanding on how genes and hormones sense and respond to nutrients normally, and what can go awry, contributing to high blood glucose levels in diabetes. The results served as the catalyst for future studies.

With the new understanding and high-impact publications, Dr. Puigserver was well-positioned to apply for additional funding from the NIH and from the American Diabetes Association, among other organizations. He is now substantially funded by the NIH and he continues to contribute significantly to the diabetes field. Dr. Puigserver has identified several chemicals that impact glucose production, and may be developed as new drugs to lower blood glucose levels in people with diabetes. For his originality and independence of thought, diabetes experts have lauded him as a major contributor and a rising star in diabetes research. In 2015, his contributions were recognized with the American Diabetes Association’s prestigious Outstanding Scientific Achievement Award.

“The American Diabetes Association Junior Faculty Award was the first major grant I received. It was a critical stepping stone for my career.”
- Jannette Dufour, PhD, Texas Tech University

“The American Diabetes Association grant was the catalyst around which my career coalesced. I have been able to leverage this strong start into a career where I am a major player in diabetes research at the national level.”
- Kieren Mather, MD, Indiana University

“The American Diabetes Association gave me my first grant to do diabetes research in 1999. Without that funding, I would not have entered the diabetes field.”
- Laura McCabe, PhD, Michigan State University
Personalized Medicine

Traditionally, medical therapies have been applied to patients in a “one-size-fits-all” approach. However, recent research advances have led scientists to the understanding that many diseases, including diabetes, are caused by a combination of many different genetic and environmental factors. In diabetes, these factors can act together to impact the insulin-producing beta cells, leading to their destruction or dysfunction. The result is high blood glucose levels and risk for complications. In short, there are many different paths that result in diabetes. Each of the factors on these paths to diabetes needs its own treatment before we can defeat diabetes for everyone.

After completion of the human genome project, “personalized medicine” was introduced as a desirable approach to health care that would take each individual’s circumstances—their known genetic risk, environment, lifestyle, age—into consideration to match the most appropriate available treatment to the personal profile.

Significant progress in personalized medicine has been realized for the treatment of many different cancers. Patients can undergo a genetic test and physicians can apply particular treatments to improve their care. Diabetes researchers are working hard to do the same for people with diabetes.

Large genome studies have identified more than 100 different genetic variations that impact a person’s risk for type 2 diabetes and about 50 genes are known to be associated with type 1 diabetes risk. Now more research is needed to determine the specific role of each of these genetic variations, how they interact with environmental factors, and what they may mean for determining ways to most effectively treat, or perhaps even prevent, diabetes in each individual.

Diabetes and Women’s Health

Applying individualized therapy approaches includes consideration of particular health risks associated with biological sex. Researchers are starting to understand how sex hormones such as testosterone and estrogen affect metabolism.

Women have increased risk for developing type 2 diabetes when estrogen function is lost, as in menopause. Furthermore, premenopausal women with type 1 diabetes are at higher cardiovascular risk than women without diabetes. Pregnant women are also subject to gestational diabetes, which increases both their own risk for developing type 2 diabetes and their children’s risks of diabetes and obesity.

The transgenerational disease risk associated with a child’s in utero environment is another area of active research supported by the American Diabetes Association. Emerging studies are showing that environmental factors, such as diet and exposure to toxins, during critical phases of fetal development can lead to poorer long-term health outcomes in offspring without regard to genetics. A mother’s high blood glucose, whether associated with type 1 or type 2 diabetes or gestational diabetes, impacts the offspring’s health. Children exposed to diabetes in utero are at ten times higher risk of developing type 2 diabetes and obesity than those who are not exposed.

Because the environment in the womb is a critical predictor of a child’s health outcomes and a large proportion of women of reproductive age have diabetes, it is increasingly important to understand how to ensure healthy pregnancies and optimal health outcomes for children born to women with diabetes during pregnancy.

Why I Support the American Diabetes Association

“Philanthropy is one of the core values for my family and we are selective about the organizations to which we give. Supporting innovative research available through the American Diabetes Association aligns with our personal interest of fighting diabetes. Diabetes runs in our family and I want answers for my children and future generations.”

– Cynthia, Philanthropic Leader

“By supporting diabetes research, it is our hope and desire that improved treatments and cures can be found. Because of our history of diabetes among the women of our family, we are especially pleased to support the Association’s women’s health programs like the ‘Fabulous You’ initiative in Baltimore, Maryland, which is designed to improve diabetes prevention and management for women.”

– Greg Kahler, President, The Kahler Foundation, Inc.
American Diabetes Association Research Programs Investments

We have been moving diabetes research forward since we funded our first research grant in 1952. In 2015 alone, we made more than $31 million in diabetes research funding available through our four major grant programs.

More than one-third of our funding supports early-career investigators, building a critical pipeline of scientists dedicated to continuing progress in diabetes. We fund the full spectrum of research related to all types of diabetes and diabetes-related disease states. Our funds support a balanced portfolio of basic fundamental research to better understand diabetes and identify new approaches to treatments and clinical research to accelerate those treatments to patients.

With special thanks for the generous gifts from people who share our passion, we did great work in 2015. With your support in 2016, we can do much more.

Make a donation to support diabetes research at diabetes.org/supportresearch or call 1-888-700-7029.