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# Type 1 Diabetes—Reaping the Rewards of a Targeted Research Investment

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**The Diabetes Control and Complications Trial (DCCT) precipitated a major research effort to develop new approaches to achieve near-normal glycemic control in real-world settings in people with type 1 diabetes. Toward that end, a unique funding stream from the U.S. Congress—the Special Statutory Funding Program for Type 1 Diabetes Research—has provided nearly \$2.5 billion for research into the prevention, cure, and treatment of type 1 diabetes since 1998. This funding generated a targeted, sustained investment in type 1 diabetes research with six specific goals: identifying new therapeutic targets through the understanding of disease etiology and pathogenesis, preventing or reversing the disease, developing cell replacement therapy, improving management and care, preventing or reducing the complications, and attracting new talent and applying new technologies to type 1 diabetes research. This Perspective describes exciting results that have emerged from the investment and further advances on the horizon, including artificial pancreas technologies, new therapies for diabetic retinopathy, and breakthroughs in laboratory production of  $\beta$ -cells. The recent program extension enables us to build on this foundation and pursue key new initiatives to harness emerging technologies and develop the next generation of type 1 diabetes researchers.**

Two decades ago, the results of the Diabetes Control and Complications Trial (DCCT) revolutionized modern-day treatment of type 1 diabetes by demonstrating that intensive glycemic control, beginning as soon as possible after diagnosis and compared with conventional care at that time, prevented or delayed the development of

complications of the eyes, kidneys, and nerves (1). This result precipitated a major research effort to develop approaches to achieve near-normal glycemic control safely in real-world settings, an effort that became increasingly urgent with subsequent demonstration of the enduring and expanding benefits of glycemic control. Over 30 years after the DCCT began, critical insights continue to emerge from this study about the importance of intensive glycemic control. Results from the DCCT follow-on study, the Epidemiology of Diabetes Interventions and Complications (EDIC) study, demonstrated that the finite 6.5-year period of intensive glycemic control provided enduring protection from later-stage microvascular complications after 30 years (2), as well as protection from cardiovascular disease (3). Recently, the EDIC study found that intensive glycemic control reduced deaths by 33% in the intensive treatment group compared with the standard treatment group (4), even though glycemic control converged to similar levels in the two groups in the two decades after the trial ended in 1993. Notably, this study found that higher average blood glucose levels and increased proteinuria were major risk factors for death, demonstrating the importance of glycemic control and reductions in diabetes complications to longer and healthier life spans for people with type 1 diabetes. These results have transformed clinical care for people with type 1 diabetes, with doctors now recommending that people with the disease practice intensive control as early in the course of the disease as safely possible. Yet despite its dramatic health benefits, early intensive glycemic control remains burdensome and elusive, making new strategies for prevention, cure, and treatment of type 1 diabetes imperative.

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## THE SPECIAL DIABETES PROGRAM FOR TYPE 1 DIABETES RESEARCH

Toward that end, the Special Statutory Funding Program for Type 1 Diabetes Research (SDP), a unique funding stream from the U.S. Congress managed by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health (NIH), provided nearly \$2.5 billion over 20 years, generating a targeted, sustained investment in high-risk, high-reward, collaborative, large-scale research with specific goals. In collaboration with the other institutes and centers of the NIH and the Centers for Disease Control and Prevention (CDC), and with input from public partnerships with JDRF, the American Diabetes Association, and the Leona M. and Harry B. Helmsley Foundation, the NIDDK has conducted a strategic planning, implementation, and evaluation process for this program to ensure the most scientifically productive use of the funds. The SDP has catalyzed and synergized the efforts of a wide range of NIH and U.S. Department of Health and Human Services (HHS) components to combat type 1 diabetes and complications, making it a model trans-NIH and trans-HHS program.

Since it was established in 1998, the SDP enabled the creation of large-scale consortia spanning prevention, treatment, and cure of type 1 diabetes and its complications that would not be possible with regular funding mechanisms. The unique SDP funding fostered high-risk, high-reward research and supported the career development of the next generation of type 1 diabetes researchers. Results from SDP-supported programs are already improving the lives of people with type 1 diabetes and are paving the way toward future successes. A number of recent exciting results from SDP-supported research illuminate the contribution this program has made in the field of type 1 diabetes research. The cumulative, wide-ranging, and scientifically consequential rewards from this program demonstrate how a targeted research investment can accelerate development of new therapies. Here, we highlight a number of recent significant findings that have emerged from the SDP and discuss new opportunities that will be pursued with the recent renewal of the program.

## ARTIFICIAL PANCREAS TECHNOLOGIES

Despite the unequivocal evidence of the benefit of early intensive glycemic control, many people, especially teens, are unable to achieve the tight control achieved in the DCCT. Population-based data from the SDP-supported SEARCH for Diabetes in Youth (SEARCH) study found one in five teenagers with type 1 diabetes have HbA<sub>1c</sub> levels above 9.5% (80 mmol/mol) (5). Data from the T1D Exchange Clinic Registry show that teenagers aged 13–17 years have a mean HbA<sub>1c</sub> of 9.0% (75 mmol/mol), and only 14% of young adults aged 18–25 years achieve an HbA<sub>1c</sub> ≤7.0% (53 mmol/mol) (6). Teenagers' mean HbA<sub>1c</sub> is closer to that achieved by the conventional

than the intensive control group in the DCCT, indicating that achieving the recommended intensive glucose control and attaining its long-term protective effects is particularly challenging in this age-group. Thus, new approaches to improve glucose control are urgently needed.

Pragmatic research to develop and test new therapies for type 1 diabetes is a high priority for the SDP. A major investment was made toward the development of an artificial pancreas—technology linking a continuous glucose monitor to an insulin pump with an algorithm that calculates and instructs delivery of an appropriate amount of insulin. Artificial pancreas technology could mitigate the major barriers to intensive glucose control: hypoglycemia and patient burden. SDP funds have been successfully deployed to support improved components of the artificial pancreas as well as a succession of studies testing their combined use, first in animals and then in people. Importantly, some controllers, key components of the artificial pancreas, have been designed to be interoperable with a variety of pumps and sensors and to use off-the-shelf smartphones as computational hubs, facilitating the continual improvement in these individual components (7). Clinical trials have progressed rapidly from short-duration studies in closely supervised conditions to multi-day use in free-living environments. Multidisciplinary teams including clinicians, bioengineers, and behavioral scientists were created to develop and test new devices, culminating in the development of improved devices that are performing well in real-world settings. One small study in adolescents found that the unsupervised, overnight use of an artificial pancreas device for 21 nights led to improved daytime and nighttime glucose control and reduced the number of episodes of nighttime hypoglycemia, even though subjects used standard glucose sensor and pump therapy during the day (8). In another study, use of an automated, bihormonal, “bionic” pancreas for 5 days and 5 nights by 21 adults and 32 adolescents led to lower mean glucose levels and reduced episodes of hypoglycemia. In fact, the bionic pancreas allowed nearly all subjects to achieve the recommended levels of glucose control (9). The U.S. Food and Drug Administration (FDA) is working closely with the NIH and investigators to facilitate this research. The NIH is now making awards for clinical trials to further expand the testing of artificial pancreas technologies in order to generate safety and efficacy data toward FDA approval of these devices.

## NEW THERAPIES FOR DIABETIC COMPLICATIONS

The targeted funding also spurred therapeutic development for microvascular complications common to both type 1 and type 2 diabetes, including studies of lower-cost generic drugs unlikely to receive industry support. With SDP support, the Diabetic Retinopathy Clinical Research Network (DRCR.net) compared three anti-vascular endothelial growth factor (VEGF) intraocular drug treatments for diabetic macular edema: Eylea (afibercept), Avastin (bevacizumab), and Lucentis (ranibizumab) (10). In this

study, Eylea was more effective at improving vision compared with Avastin and Lucentis in people whose starting vision was 20/50 or worse. Patients with milder vision loss, who comprised half the study population, also had substantial visual acuity improvement, but results were similar with all three anti-VEGF treatments. No major differences in the safety of the three drugs were found. On the basis of Medicare allowable charges, the per-injection costs of each drug at the doses used in this study were about \$1,960 for Eylea, about \$1,200 for Lucentis, and about \$70 for Avastin; most patients required 10–12 injections. Thus, these results offer important data for informing clinical decisions and personalizing treatment for diabetic macular edema and also have significant cost implications. Another key finding from the study is that anti-VEGF therapy actually improves vision, as compared with laser treatment that is effective in preventing blindness but does not improve vision and often somewhat worsens it in the short term. Improving vision with anti-VEGF therapy can make the difference between people being able to drive or not, which greatly affects quality of life.

The NIH and SDP roles in this study are noteworthy as the private sector is unlikely to undertake the comparison of drugs from different companies with large cost savings. Another new clinical trial not of interest to the pharmaceutical industry is the testing of the generic gout drug allopurinol for the preservation of kidney function in people with type 1 diabetes at high risk of kidney disease. Despite the efficacy of glucose and blood pressure control and ACE blockade in reducing the risk of diabetic nephropathy, rates of diabetic nephropathy remain high. Moreover, no new therapy has emerged in the past two decades. On the basis of strong preliminary data, a multicenter trial of allopurinol to slow the progression of nephropathy in type 1 diabetes was recently launched by the Preventing Early Renal Loss in Diabetes (PERL) Consortium with full support by the SDP (11). If this safe and inexpensive drug proves effective, allopurinol may also be relevant to renal protection in the larger population with type 2 diabetes.

### RESTORING $\beta$ -CELL FUNCTION

Another strategic goal pursued with the special funding is to identify ways to replace lost  $\beta$ -cells and restore insulin production. Islet transplantation has been demonstrated to be highly successful in reversing hypoglycemia unawareness (12). The Immune Tolerance Network (ITN), with SDP support, conducted the first international, multicenter trial of islet transplantation using the Edmonton protocol (13). Building on this trial, the Clinical Islet Transplantation (CIT) Consortium, supported by the SDP, has conducted clinical and mechanistic studies in islet transplantation, with or without accompanying kidney transplantation, with a goal of validating a process for islet cell manufacturing for submission to the FDA for licensure as a biologic product. If the licensure is approved, islet transplantation could potentially transition from an experimental treatment to a procedure covered by third-party

insurers. The islet-alone phase 3 trial has been completed, and the islet-after-kidney phase 3 trial has reached its primary end point. In addition, the Collaborative Islet Transplant Registry (CITR), also supported with SDP funding, found that rates of independence from insulin administration at 3 years after islet transplant increased over time—from 27 to 37 to 44% in 1999–2002, 2003–2006, and 2007–2010, respectively (14). The transplanted islets also functioned longer in the most recent period, and the procedure protected patients from severe episodes of hypoglycemia. In addition to demonstrating that islet transplantation can achieve insulin independence, results from the phase 3 trials and CITR show that even if insulin therapy is required, islet transplantation allows recipients previously incapacitated by hypoglycemia to achieve glycemic targets with a sustained marked decrease in severe hypoglycemic episodes. While this treatment has been life-changing for those with severe, recurring episodes of hypoglycemia, its use is limited by side effects of immunosuppressive medications and limited numbers of donor islets.

The Beta Cell Biology Consortium (BCBC) was established, with SDP support, to facilitate interdisciplinary collaborations to advance the understanding of pancreatic islet development and function with the goal of developing innovative therapies to correct the loss of  $\beta$ -cell mass in diabetes, including cell reprogramming, regeneration, and replacement. This team science initiative brought together more than 50 research laboratories. Their efforts contributed to one of the most important advances in stem cell biology—the recent discovery of a method for large-scale production of glucose-responsive  $\beta$ -cells from human pluripotent stem cells (15). This breakthrough brings us closer to the goal of  $\beta$ -cell replacement through transplantation and has accelerated efforts to protect newly transplanted  $\beta$ -cells from the autoimmune attack through encapsulation, as well as immunomodulation. In addition, BCBC researchers discovered that  $\delta$ -cells could be reprogrammed into  $\beta$ -cells, representing another potential way to restore lost  $\beta$ -cells in type 1 diabetes (16).

Building on this progress, the newly launched Human Islet Research Network (HIRN) (<http://hirnetwork.org>) will pursue innovative strategies to protect and replace  $\beta$ -cells in people with diabetes. Four independent, but complementary, research initiatives are focused on specific goals using human cells and tissues. One consortium is focused on the discovery of highly specific biomarkers of  $\beta$ -cell injury that will be important for testing strategies to stop  $\beta$ -cell destruction early in the disease process. Another is combining advances in  $\beta$ -cell and stem cell biology with tissue engineering technologies to develop microdevices that will support functional human islets in vivo. A third is developing innovative approaches to model the immunobiology of type 1 diabetes, reconstructing the disease using induced pluripotent stem cell-derived  $\beta$ -cells and thymic epithelial cells and immune systems

derived from people with type 1 diabetes implanted in immunodeficient mice. The fourth is investigating methods to increase or maintain functional  $\beta$ -cell mass through targeted manipulation of islet plasticity or engineered protection of  $\beta$ -cells.

### ELUCIDATING THE CAUSES OF TYPE 1 DIABETES

Type 1 diabetes arises through an interaction between genetic predisposition and environmental factors. The HLA region on chromosome 6p21.3 is by far the strongest genetic determinant for type 1 diabetes, accounting for about 50% of the genetic risk. Through the SDP-funded international Type 1 Diabetes Genetics Consortium (T1DGC) more than 50 additional chromosomal regions have been identified that harbor loci that confer low to moderate risk of developing type 1 diabetes (17). This effort has made type 1 diabetes rare among polygenic diseases in that more than 80% of the genetic risk is accounted for by known loci. Building on this success, SDP funds will support research to elucidate the specific genes and mechanisms involved, providing potential new therapeutic targets. Already an SDP-supported study found that *Clec16a*, a type 1 diabetes susceptibility gene, is required for normal glucose-stimulated insulin release (18). The diabetogenic single nucleotide polymorphism reduces insulin secretion in humans, and pancreatic deletion of *Clec16a* alters mitochondria in islets and induces  $\beta$ -cell endoplasmic reticulum stress. This work uncovered an important role for mitophagy in  $\beta$ -cell function and a pathway that could be a therapeutic target for type 1 diabetes prevention.

New impetus for identifying environmental determinants of type 1 diabetes has come from the SEARCH study. With SDP support, the SEARCH study reported the first national surveillance data on rates of childhood diabetes. The study found that the prevalence of type 1 diabetes in people under age 20 years rose by 21% between 2001 and 2009, and the incidence of childhood type 1 diabetes increased on average 2.7% annually (19). This increase is nearly as rapid as that seen in northern Europe and without evidence of the plateau seen after 2005 in Europe. This suggests that an environmental factor(s) contributes to disease risk. Identifying dietary, infectious, or other environmental triggers or protective factors is critical to understanding the disease process and to developing prevention strategies.

Soon after the inception of the SDP, the NIH launched The Environmental Determinants of Diabetes in the Young (TEDDY) study to identify such triggers or protective factors (20). The availability of tests for genetic risk and assays to measure onset of autoimmunity made such a study possible. Capitalizing on this opportunity, 450,000 newborns were screened to identify and enroll over 8,000 at high genetic risk for type 1 diabetes. Participants are developing autoimmunity and type 1 diabetes at the rates predicted, with follow-up planned through age 15 years. Detailed information on diet, infections, and other

environmental exposures are being analyzed. Recently, TEDDY launched case-control studies probing some of the over 2.7 million biological samples collected to date with state-of-the-art genomic, metabolomic, and proteomic technology to answer critical questions about disease etiology. It also provides an unparalleled resource to study the development of the human microbiome from birth through childhood. The detailed information collected in the study has already shed light on the pathogenesis of celiac disease, a more common condition that shares risk genes with type 1 diabetes (21).

### TESTING STRATEGIES TO PREVENT AND DELAY TYPE 1 DIABETES

Even while awaiting new approaches to type 1 diabetes prevention that are anticipated to emerge from TEDDY, another international consortium is testing strategies for the prevention or delay of type 1 diabetes based on the current understanding of the disease, our ability to define the level of risk for type 1 diabetes in asymptomatic individuals, and the results of previous intervention studies suggesting potential efficacy. Type 1 Diabetes TrialNet (TrialNet) evolved from the Diabetes Prevention Trial-Type 1 (DPT-1), which tested whether two separate interventions involving insulin could prevent the progression from autoimmunity to type 1 diabetes. Although protective effects of insulin were not demonstrated, DPT-1 did show in a large cohort that diabetes risk over 5–10 years could be accurately determined in people with autoimmunity from families with type 1 diabetes (22,23). Accurate risk assessment is essential for the design of studies to prevent or delay the disease and is particularly important as these studies involve children and interventions with some potential for adverse effects. The DPT-1 Risk Score (DPTRS) has now been studied using TrialNet Natural History Study data and has been found to improve type 1 diabetes risk classification accuracy (24). Data from DPT-1, TrialNet, and other studies form the basis for a new recommendation from JDRF, the Endocrine Society, and the American Diabetes Association for a type 1 diabetes staging classification in at-risk individuals that provides a framework for the research and development of preventive therapies (25). TrialNet, also supported by the SDP, has screened over 100,000 relatives of people with type 1 diabetes to identify subjects for trials testing strategies for prevention of progression from autoimmunity to type 1 diabetes.

Three prevention trials are ongoing in TrialNet, oral insulin, anti-CD3 monoclonal antibody (teplizumab), and CTLA-4-Ig (abatacept); one is based on a previous prevention study and two are based on promising results in preserving  $\beta$ -cell function in newly diagnosed type 1 diabetes. In DPT-1, oral insulin caused a significant delay of type 1 diabetes onset in a subgroup of subjects with high titers of insulin autoantibodies (22); this post hoc observation is being tested by TrialNet. Treatment with teplizumab was previously shown to slow the decline

in C-peptide production after 2 years in patients with new-onset diabetes (26). The TrialNet teplizumab study will test whether progression to type 1 diabetes can be prevented or delayed in subjects with two autoantibodies and impaired glucose tolerance. This is the first example of a trial to test a nonantigen-specific immunomodulatory agent in type 1 diabetes prevention. The TrialNet study of abatacept in newly diagnosed patients found that 2 years of monthly drug treatment delayed C-peptide decline (27). Moreover, treatment effects persisted for 1 year after the drug was discontinued (28). Abatacept was approved by the FDA as a therapy for rheumatoid arthritis in 2005, illustrating how research in one autoimmune disease can contribute to progress in others. The teplizumab and abatacept prevention trials represent a paradigm in which the efficacy and safety profile of these agents in new-onset type 1 diabetes trials propel testing them earlier in the disease course. Subsequently, such drugs may be studied in combination. If successful, these high-risk, high-reward studies may inform critical future public health efforts to identify those at risk and to intervene to prevent type 1 diabetes.

### FOSTERING THE NEXT GENERATION OF RESEARCHERS

The SDP has also been used to foster training and career development for investigators in type 1 diabetes research. The Type 1 Diabetes Pathfinder Award supported exceptional new investigators who proposed creative new research approaches that have the potential to produce a major impact on important problems in biomedical and behavioral research relevant to type 1 diabetes and its complications. Ten awards were made in 2008 spanning research in basic immunology, diabetes complications, islet encapsulation, cell-based therapy, and molecular approaches to restoring glycemic control in type 1 diabetes. All 10 awardees remain active in diabetes research, with the majority obtaining subsequent NIH grant support as a principal investigator. Similarly successful are the Career Development Programs in Diabetes Research for Pediatric Endocrinologists that support pediatric endocrinologists in their transition to an independent research career. Of the 28 pediatric endocrinologists who have completed the program, 27 remain in academic medicine as of 2014. Recent renewal of the SDP will provide for expansion of these programs.

The progress described above required multidisciplinary collaborations and novel approaches. The SDP funding has been used to attract new and diverse talent to meet specific needs in type 1 diabetes research. For example, the funds have supported opportunities for bioengineers to collaborate with diabetes researchers on projects ranging from the artificial pancreas to islet encapsulation. The SDP is also supporting the training of behavioral scientists and research collaborations to conduct research relevant to improved clinical management and quality of

life for people with type 1 diabetes. SDP support has also attracted leading proteomics, metabolomics, microbiome, and biocomputational researchers to apply their expertise to the analysis of the biosamples and data collected in TEDDY.

### EMERGING OPPORTUNITIES IN TYPE 1 DIABETES RESEARCH

With the recent extension of the SDP for fiscal years 2016 and 2017 at \$150 million per year, the NIDDK embarked on a planning process to identify new and emerging opportunities in type 1 diabetes and its complications. Members of the federal Diabetes Mellitus Interagency Coordinating Committee (DMICC) were invited to submit research proposals for the renewed funding. At a 2-day meeting in April 2015, representatives from the NIH and CDC presented over 40 proposals to a panel of 21 scientific experts and a public representative. The panel was asked to provide input to NIDDK leadership on the proposals, including whether each proposal represented the best use of the funds. Ongoing projects, such as those described here, were presented in addition to novel programs. Panel members were also encouraged to identify

**Table 1—Active fiscal years 2016 and 2017 Funding Opportunity Announcements supported by the SDP**

#### Artificial pancreas technologies

- Advanced Clinical Trials to Test Artificial Pancreas Device Systems in Type 1 Diabetes (RFA-DK-16-008)
- Small Business Innovation Research (SBIR) to Develop New or Improved Closed Loop Automated Technologies for Diabetes Therapy and Monitoring (RFA-DK-15-022)
- Clinical, Behavioral and Physiological Research Testing Current and Novel Closed Loop Systems (RFA-DK-16-009)

#### Diabetes complications

- Research Using Biosamples and Subjects From Type 1 Diabetes Clinical Studies—Complications (RFA-DK-15-019)

#### Elucidating the causes of type 1 diabetes

- Mechanisms Underlying the Contribution of Type 1 Diabetes Risk-Associated Variants (RFA-DK-15-025)
- Understanding the Pathogenesis and Etiology of Type 1 Diabetes Using Biosamples and Subjects From Clinical Studies (RFA-DK-15-018)
- Limited Competition: Understanding How Epigenetics and Infections Impact Autoimmunity and Diabetes in The Environmental Determinants of Diabetes in the Young Study (TEDDY) (RFA-DK-15-506)

#### Testing strategies to prevent and delay type 1 diabetes

- Small Business Innovation Research (SBIR) to Develop New Methods and Technologies for Assessment of Risk and for Early Diagnosis and Prognosis of Type 1 Diabetes (T1D) (RFA-DK-15-024)

#### Fostering the next generation of researchers

- Career Development Programs in Diabetes Research for Pediatric Endocrinologists (RFA-DK-15-006)
- Type 1 Diabetes Pathfinder Award (RFA-DK-15-030)

#### Improving management of type 1 diabetes

- Impact of the Use of Glucose Monitoring and Control Technologies on Health Outcomes and Quality of Life in Older Adults With Type 1 Diabetes (T1D) (RFA-DK-15-028)

**Table 2—Planned Funding Opportunity Announcements for fiscal years 2016 and 2017 supported by the SDP\*****Diabetes complications**

- Neurocognitive effects of glycemic dysregulation in type 1 diabetes
- Continuation of PERL—a multicenter clinical trial of allopurinol to prevent glomerular filtration rate loss in type 1 diabetes

**Restoring  $\beta$ -cell function**

- Small Business Innovation Research development of new technologies and bioengineering solutions for the advancement of cell replacement therapies for type 1 diabetes
- Continuation of the Integrated Islet Distributed Program
- Continuation of the CITR

**Elucidating the causes of type 1 diabetes**

- Continued follow-up of subjects and immunological assessments in TEDDY

**Pathogenesis of type 1 diabetes**

- Surveillance for type 1 diabetes among young adults
- Continuation of SEARCH study
- Human Pancreas Procurement and Analysis Program

**Testing strategies to prevent and delay type 1 diabetes**

- Continuation of Type 1 Diabetes TrialNet Data Coordinating Center

**Improving management of type 1 diabetes**

- Improving adherence in young children with type 1 diabetes
- Improving adherence in preteens, adolescents, and young adults with type 1 diabetes
- Understanding barriers and facilitators to type 1 diabetes management in adults
- Continuation of programs for standardization of C-peptide and HbA<sub>1c</sub> assays

\*Note that not all SDP-supported projects that will be active in fiscal years 2016 and 2017 are shown in the table because many ongoing programs will not require new Funding Opportunity Announcements.

gaps in existing programs and to suggest potential new areas of research interest. This meeting provided critical input to the NIDDK and is valuable to the planning process for the SDP. The panel members were enthusiastic about many programs and research consortia currently supported by the SDP and strongly endorsed future plans to continue and expand ongoing efforts. For example, research to develop and test new or improved closed-loop technologies should incorporate behavioral research and address the needs of specific populations such as adolescents and older adults. The panel encouraged the development of new strategies to prevent or reverse complications, including studies of neurocognitive function in type 1 diabetes. Because people with type 1 diabetes are now living longer and healthier lives as a result of research, there is also a need to study the disease across the life span. This valuable input, as well as that received at other scientific meetings, assisted the NIDDK in its planning efforts to make the best use of the additional funds. The resulting active and anticipated Funding Opportunity Announcements for fiscal years 2016 and 2017 are detailed in Tables 1 and 2,

respectively. A meeting summary will be posted on the SDP website ([www.t1diabetes.nih.gov](http://www.t1diabetes.nih.gov)). With the significant progress that has been achieved in type 1 diabetes research, there is an abundance of scientific opportunities that can be pursued, and more are expected in the coming years.

**SUMMARY**

These advances, supported in part or in whole by the SDP, underscore how a targeted and sustained investment in type 1 diabetes research has enabled tremendous progress. As we celebrate the significant progress made to improve the lives of people with type 1 diabetes, we look forward to reaping additional rewards as the ongoing research investments come to fruition. This targeted investment has laid the groundwork for future advances toward a cure through  $\beta$ -cell replacement and ultimately toward prevention of the disease in those at risk.

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