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"Progress Toward a Cure for Type I Diabetes: Research and the Artificial Pancreas"

Statement of

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Chairman Collins, Ranking Member Casey, and Members of the Committee, as Director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), thank you for your invitation to testify at this hearing on type 1 diabetes. On behalf of NIDDK and the other Institutes and Centers of the National Institutes of Health (NIH) within the U.S. Department of Health and Human Services (HHS), I am pleased to tell you about some of the significant recent scientific advances and future research opportunities in type 1 diabetes and its complications, including research supported by the *Special Statutory Funding Program for Type 1 Diabetes Research* (*Special Diabetes Program*).

Today I would like to update you on the following topics: improving the outlook for people with type 1 diabetes; developing technologies to improve glucose control; restoring beta cell function; preventing, treating, and reversing diabetic complications; understanding the causes of type 1 diabetes toward disease prevention; testing strategies to stop the autoimmune attack and preserve beta cells; and emerging opportunities in type 1 diabetes research.

The economic and personal toll diabetes takes on our nation is substantial, and biomedical research holds the promise to prevent, treat, and ultimately cure this disease. Toward improving the health of Americans affected by diabetes, NIH invests more than $1 billion a year in diabetes research. This investment has been complemented by the support and efforts of our research partners—academic institutions, the U.S. Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC), and charitable and patient advocacy groups such as JDRF (formerly the Juvenile Diabetes Research Foundation), the American Diabetes Association (ADA), and the Leona M. and Harry B. Helmsley Charitable Trust, who share our goals to prevent, treat, and cure type 1 diabetes.

Through the invaluable support of Congress, through collaborative and coordinated research efforts, through the hard work of our researchers, and through the dedication and generosity of our clinical research participants, we have made important strides toward these goals.

Type 1 diabetes primarily strikes children and adolescents, but it may begin at any age. It is an autoimmune disease, in which the body's immune system launches a misguided attack and destroys the insulin-producing beta cells found in clusters called islets within the pancreas. Insulin is an essential hormone that helps the body regulate glucose (sugar) levels in the blood. Because their bodies no longer produce insulin, people with type 1 diabetes—or the parents of young children with the disease—must do the work of the lost beta cells. The children here today and people of all ages with the disease must closely watch their food intake and physical activity levels, monitor their blood glucose levels many times each day and night, and administer insulin through injections or an insulin pump. This is an enormous and relentless burden on them and their families, and greatly affects quality of life. Despite their vigilance, people with type 1 diabetes remain susceptible to dangerous and frightening episodes of hypoglycemia (low blood glucose) and to developing long-term complications that affect their eyes, kidneys, nerves, heart, and other organs. Thus, it is imperative to pursue research to identify prevention strategies and improved treatments, while striving for a cure.

IMPROVING THE OUTLOOK FOR PEOPLE WITH TYPE 1 DIABETES

Biomedical research has led to dramatic improvements in the health and quality of life of people with type 1 diabetes. A major contributor to this success is the information that has been garnered by the NIDDK's landmark Diabetes Control and Complications Trial (DCCT) and its follow-up study, the Epidemiology of Diabetes Interventions and Complications (EDIC). DCCT, which began in 1983, compared the effect of intensive blood glucose control versus what was conventional care at the time on the long-term health of people with type 1 diabetes. DCCT demonstrated that intensive control, beginning as soon as possible after diagnosis, prevented or delayed the development of complications of the eyes, kidneys, and nerves. After DCCT ended in 1993, EDIC—which began in 1994 and is ongoing—followed the original DCCT participants and demonstrated enduring protective effects of intensive glucose control on the eye, kidney, nerve, and heart complications of diabetes. These results transformed clinical care for people with type 1 diabetes: doctors now recommend that people with the disease practice intensive control as early in the course of the disease as safely possible.

Even though it has been nearly 35 years since DCCT began, this important study continues to provide critical insights. The study recently reported results related to diabetic eye disease (retinopathy), showing that people with type 1 diabetes who intensively control their blood glucose early in their disease, versus those who do not, are 48 percent less likely to need eye surgery, which reduced eye surgery costs.[1] This reduction led to eye surgery costs about 32 percent lower for people who practice early intensive glucose control. Another important recent eye finding came from analysis of about 24,000 eye exams from over three decades: DCCT/EDIC scientists determined that people with type 1 diabetes should get eye exams to detect retinopathy based on their risk, rather than on an automatic, annual schedule.[2] Adjusting the frequency of eye screenings to a personalized approach—based on risk of severe eye problems—would result in fewer eye exams at lower cost and quicker diagnosis. For example, over 20 years, the new schedule would result in eight exams on average, a greater than 50 percent reduction in eye examinations compared with annual exams.

DCCT/EDIC researchers also examined differences in cardiovascular (heart) problems, which can take many years to develop, and found that those who practiced early intensive blood glucose management had a 30 percent reduced incidence of cardiovascular disease and 32 percent fewer major cardiovascular events 30 years later.[3] Historically, people with type 1 diabetes have had a higher mortality rate than the general population. In another advance, DCCT/EDIC researchers recently found that this increased mortality rate can be reduced or eliminated through careful management of blood glucose.[4] These new findings add to DCCT/EDIC's decades of evidence demonstrating that people with type 1 diabetes can dramatically increase their likelihood of living long, healthy lives by practicing early, intensive blood glucose management. They also demonstrate the fruits of a long-term research investment—NIDDK has supported DCCT/EDIC for nearly 35 years.

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[1] https://www.ncbi.nlm.nih.gov/pubmed/25923552
[2] https://www.ncbi.nlm.nih.gov/pubmed/28423305
[3] https://www.ncbi.nlm.nih.gov/pubmed/26861924
[4] https://www.ncbi.nlm.nih.gov/pubmed/27411699

DEVELOPING TECHNOLOGIES TO IMPROVE GLUCOSE CONTROL

Results from DCCT/EDIC clearly show the importance of good glucose control to the long-term health of people with type 1 diabetes. Type 1 diabetes, however, is an extremely burdensome disease to manage for even the most vigilant, and intensive therapy brings with it potentially dangerous episodes of hypoglycemia. Thus, despite the unequivocal evidence of benefit, many people, especially teens, are not able to achieve the level of glucose control that researchers helped DCCT participants achieve. Data from the SEARCH for Diabetes in Youth study, co-led by CDC and NIDDK, showed that one out of five teenagers with type 1 diabetes have hemoglobin A1c (HbA1c) levels—a measurement of blood glucose levels over time—above 9.5 percent, which is above the 9.0 percent average level of the DCCT group that did not practice intensive control, and much higher than the recommended level for adolescents of less than 7.5 percent.[5] This is worrisome, indicating that achieving the recommended intensive glucose control and attaining its long-term protective effects is particularly challenging in this age group. Because poor glucose control may worsen the long-term health of these children, new approaches to improve glucose control are urgently needed.

NIDDK has invested significantly with resources provided by the *Special Diabetes Program* in glucose management technology, including artificial pancreas technologies. An artificial, or bionic, pancreas has three components: a glucose-sensing component that measures blood glucose levels and sends data to a computer; an insulin delivery device; and a computer that calculates the amount of insulin needed and instructs insulin delivery based on that calculation, thereby "closes the loop" between glucose sensing and insulin delivery. This technology is designed to do the work of the pancreas with minimal human input, and holds promise not only to relieve patient and caregiver burden, but also to improve the health of people with type 1 diabetes. A significant milestone was achieved last fall when the FDA approved the first commercial hybrid artificial pancreas device.[6] NIDDK supported early research that contributed to the development of the approved device, and continues to vigorously support research at all stages to advance artificial pancreas technology.

The commercial artificial pancreas device that FDA approved last fall is a first-generation hybrid device intended for insulin delivery and continuous glucose monitoring in people ages 14 and older with type 1 diabetes. The device can be programmed to automatically adjust insulin administration; however, it still requires users to count and enter mealtime carbohydrates. An NIDDK-supported study of day and night use of another hybrid artificial pancreas device at home, without continuous monitoring by study staff, found that such use was feasible and safe in adolescents, and that it increased the amount of time these adolescents spend in the target blood glucose range.[7] The component of this device that calculates insulin requirement based on glucose sensing is designed to work with numerous sensors and pumps, so that it could potentially work with improved versions of these sensor and pump components that are subsequently developed. Numerous improvements are on the horizon which could more fully automate artificial pancreas technology, make the devices simpler and more user friendly,

[5] https://www.ncbi.nlm.nih.gov/pubmed/19643434
[6] https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm522974.htm
[7] https://www.ncbi.nlm.nih.gov/pubmed/26740634

personalize care and expand the user population for this technology. It is imperative to continue pursuing additional artificial pancreas technologies through research to reach these goals, and NIDDK-supported development of many other devices is progressing rapidly. For example, the first at-home study of a bihormonal pancreas system—one which delivers both insulin and glucagon, hormones that work together to control blood glucose levels—showed that it improved glucose control better than conventional insulin pump therapy without the need for carbohydrate counting before mealtimes.[8]

The successes of these and other studies have laid the groundwork for more advanced clinical trials to generate data toward FDA approval of these devices. NIDDK, through the *Special Diabetes Program*, is supporting four new such trials that have recently begun recruitment or will begin recruiting in the next year. These pivotal studies will test the artificial pancreas technologies in larger groups, with wider age ranges, over longer periods of time, and in real world conditions. They will look at factors including safety, efficacy, user friendliness, physical and emotional health of participants.

Two of the trials build on the advances described above: one trial will test the bihormonal artificial pancreas system in 600 people, including children as young as four years of age, for six months. A second trial will test artificial pancreas use in 130 youth ages six to 18 for a full year. The third trial being supported is a trial that will compare the currently FDA-approved hybrid closed loop artificial pancreas device to a next-generation system, further refined to improve blood glucose control, particularly around mealtime, in 100 youth for three months. A fourth set of studies will test an innovative platform on smartphones with different insulin pumps and state-of-the-art glucose sensors. These trials are intended to advance the goal to have multiple artificial pancreas technologies that are FDA-approved for use in all ages, allowing people with type 1 diabetes, their caregivers, and their healthcare providers to choose the technology best suited to their needs.

NIDDK continues to support research being conducted by small businesses to develop innovative technologies to improve the components of artificial pancreas devices. For example, one small business supported by NIDDK created a computer program that runs on a mobile device linked to an insulin pump and continuous glucose monitor. The development of this technology was initially supported by grants to an academic investigator and then to the small business. The program was recently selected as the core analytic and control technology for a device in one of the new advanced trials described above.

We also support research to identify the most effective ways to incorporate artificial pancreas technologies into clinical care and how to enhance the usability of these new tools to help patients in their decision making regarding diabetes control, without overwhelming them with excessive data or complexity. Recently, the FDA expanded the approved use of one brand of continuous glucose monitor indicated for management of diabetes in people two years and older, enabling people to make diabetes treatment decisions using data from this device without confirming glucose levels with a painful finger stick.[9] This continuous sensor device is also

[8] https://www.ncbi.nlm.nih.gov/pubmed/28007348
[9] https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm534056.htm

being studied as part of an automated artificial pancreas. Partnerships between bioengineers designing these devices, clinicians, and behavioral scientists are key to making artificial pancreas use easier. With continued research, artificial pancreas technology may become a reality for all people with type 1 diabetes.

RESTORING BETA CELL FUNCTION

Although artificial pancreas technology represents an important and near-term approach to managing type 1 diabetes, it is not a cure. Thus, another major goal of NIH-supported type 1 diabetes research is to identify ways to replace lost beta cells and thereby restore insulin production—a biological cure for the disease. One way to restore the ability to produce insulin in response to glucose levels is to replace beta cells through islet transplantation. The current procedure involves purifying islets from a donor pancreas and transplanting them into a person with type 1 diabetes. NIDDK and the National Institute of Allergy and Infectious Diseases' (NIAID) co-led Clinical Islet Transplantation (CIT) Consortium, supported by the *Special Diabetes Program*, has been conducting clinical and mechanistic studies to test different strategies to make islet transplantation safer and more effective. One of CIT's trials, a Phase III study of islet transplantation without accompanying kidney transplantation, tested islet transplantation in 48 people with type 1 diabetes who had persistent impaired awareness of hypoglycemia and frequent severe hypoglycemia events despite expert care. For this select group of people with difficult-to-control diabetes and very high risk, frequent life-threatening hypoglycemic events, the potential benefits of this procedure could outweigh the risks of having to take immunosuppressive medicines following such a transplant.

The study found that, two years after transplantation, more than 70 percent of participants were free of severe hypoglycemic events, had established near-normal control of glucose levels, and had restored hypoglycemia awareness.[10] These findings are significant, indicating that islet transplantation is an effective treatment for people whose type 1 diabetes cannot be controlled by other means and for whom hypoglycemic episodes are life-threating. The results of this trial will be the basis for applications to the FDA for licensure of purified human pancreatic islets; licensure would allow third-party reimbursement for the pancreatic islets used during the transplant procedure, transitioning it from an experimental drug to one covered by insurers.

One barrier to islet transplantation is the scarcity of donor islets for transplant. Toward overcoming this barrier and pursuing other innovative strategies to protect and replace beta cells in people with diabetes, NIDDK launched the Human Islet Research Network (HIRN) with support from the *Special Diabetes Program*. HIRN builds on the ground-breaking successes of NIDDK's Beta Cell Biology Consortium, which focused primarily on research in mice. Now advances from the Beta Cell Biology Consortium are being incorporated into HIRN's studies of human beta cells. For example, researchers in HIRN developed a new laboratory production method to make large quantities of beta cells from the skin cells of people with type 1 diabetes.[11] This method could, with further development, be used to manufacture beta cells from a person with type 1 diabetes in the quantities needed for transplantation back into that same person. These cells would likely require protection from autoimmune attack, perhaps through a

[10] https://www.ncbi.nlm.nih.gov/pubmed/27208344
[11] https://www.ncbi.nlm.nih.gov/pubmed/27163171

bioengineered approach to encapsulation of cells, but the recipient might not require toxic immunosuppressive medications to prevent rejection of the tissue. This procedure for generating beta cells and islets from skin cells could also provide a valuable resource for drug screening and for precision medicine studies of the development of the disease.

HIRN scientists are exploring other strategies for replacing the lost beta cells, such as replication of a patient's remaining beta cells or regeneration of beta cells from related cells in the body, without the need for transplantation. Small molecules—which can be developed into drugs—hold promise for inducing beta cell replication or regeneration, and HIRN is contributing to exploration of this possibility. Scientists are identifying and studying such small molecules, like harmine[12] and SerpinB1,[13] as well as generating new small molecule screening assays,[14] to discover and develop highly potent, beta cell-specific molecules.

HIRN researchers have also made exciting progress in identifying biomarkers of beta cell death and in developing the means to measure these markers in people with type 1 diabetes.[15,16,17] For example, using the knowledge that dying cells release fragmented DNA into the blood, researchers demonstrated that beta cells release DNA with a uniquely modified pattern that can be detected in people with type 1 diabetes. At present, this research indicates these assays are sensitive enough to reliably monitor the success or failure of transplanted islets in humans, giving us a valuable new tool in transplantation research. The next generation of assays, which are in development, are designed to be even more sensitive, and could potentially detect the loss of only a very few beta cells early in the disease process, possibly before any other clinical signs can be detected. These advances could lead to a minimally invasive approach to monitor people at risk for the disease and to diagnose type 1diabetes much earlier, perhaps when the process of beta cell loss could be halted and overt disease prevented.

PREVENTING, TREATING, AND REVERSING DIABETIC COMPLICATIONS

Pursuing these promising directions for replacing lost beta cells is imperative, since chronic elevation of blood glucose levels slowly damages organs and can result in life-threatening diabetes complications. SEARCH recently reported estimates that by about age 21, approximately 32 percent of youth with type 1 diabetes would have at least one complication for the disease or would be at high risk for a complication.[18] This finding scares us all, and underscores the need for early monitoring of youth for earlier diagnosis and treatment of complications, and the critical need to pursue research toward preventing, treating, or reversing diabetes complications.

Blindness is a debilitating complication of diabetes. Laser treatment can be an effective therapy to prevent blindness in advanced cases of diabetic eye disease or vision loss from diabetic macular edema (DME), a type of diabetic eye disease. This treatment, however, causes

[12] https://www.ncbi.nlm.nih.gov/pubmed/25751815
[13] https://www.ncbi.nlm.nih.gov/pubmed/26701651
[14] https://www.ncbi.nlm.nih.gov/pubmed/27624103
[15] https://www.ncbi.nlm.nih.gov/pubmed/26976580
[16] https://www.ncbi.nlm.nih.gov/pubmed/27643615
[17] https://www.ncbi.nlm.nih.gov/pubmed/26216854
[18] https://www.ncbi.nlm.nih.gov/pubmed/28245334

some immediate and permanent scarring of the eye and worsening of vision in order to prevent future events that could cause blindness. This prompted scientists in the National Eye Institute-led Diabetic Retinopathy Clinical Research Network (DRCR.net) to seek better treatments. In 2010, a landmark DRCR.net trial demonstrated that an anti-vascular endothelial growth factor (VEGF) drug, ranibizumab injection, is a more effective treatment for DME than laser treatment.[19] This finding dramatically changed clinical practice, and ranibizumab injection quickly became one of the standard treatments for people with vision loss from DME.

Building on this result, a recent DRCR.net comparative effectiveness trial compared safety and efficacy of three anti-VEGF drugs commonly used to treat DME: Eylea® (aflibercept), Avastin® (bevacizumab), and Lucentis® (ranibizumab injection). The trial showed that, in people with DME and mild visual impairment, any of the three drugs, on average, improved visual acuity and that the drugs were equally effective after two years.[20] These results give people with diabetes and their providers more options for treating DME, specifically regarding the cost of treatment. Improving vision with anti-VEGF therapy can make the difference between being able to drive or not, which greatly affects quality of life.

DRCR.net also showed, in a separate trial, that ranibizumab was more effective than laser treatment at improving visual acuity over two years for eyes with the most severe form of diabetic eye disease—proliferative diabetic retinopathy.[21] This result gave people with diabetes and their providers the first new option for treating proliferative diabetic retinopathy in four decades. Eyes treated with ranibizumab also had fewer complications from diabetic retinopathy and required less eye surgery. In April, based on these results, FDA approved ranibizumab for all forms of diabetic retinopathy, expanding the previous approval of the drug for people with DME.[22]

With support from the *Special Diabetes Program*, the Preventing Early Renal Loss in Diabetes (PERL) trial is studying whether the inexpensive, generic medication allopurinol, currently used for treating gout, can preserve kidney function in people with type 1 diabetes who are at high risk of kidney disease. PERL recently finished recruitment and, if this inexpensive drug proves effective, it has the potential to be the first new therapy to reduce risk for diabetic kidney disease in over two decades.

UNDERSTANDING THE CAUSES OF TYPE 1 DIABETES TOWARD DISEASE PREVENTION

In parallel to efforts to improve management of type 1 diabetes, develop a cure, and prevent or treat diabetic complications, it is imperative to gain better understanding of the initiation and earlier stages of the disease. This will enable us to develop prevention strategies, so future generations do not have to be burdened with the disease like the children and adults here today are. A person's risk for developing type 1 diabetes involves both genetic and

[19] https://www.ncbi.nlm.nih.gov/pubmed/20427088
[20] https://www.ncbi.nlm.nih.gov/pubmed/26935357
[21] https://www.ncbi.nlm.nih.gov/pubmed/26565927
[22] https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2017/125156orig1s114ltr.pdf

environmental factors. Many genes are known to contribute to disease risk, but environmental factors are not yet conclusively identified. Knowing these factors and determining their contributions is key to understanding the causes of type 1 diabetes.

We have made significant progress in understanding the genetic contributors to type 1 diabetes. Only a decade ago, just a few genes that increased risk for the disease had been identified. Today, because of NIDDK's Type 1 Diabetes Genetics Consortium and other groups, we know over 50 genes or genetic regions that affect disease risk, representing about 80 percent of the genetic contributors. To build on this success, NIDDK is supporting research to understand the function of identified genes to determine how they may influence disease development, which could lead to new targets for prevention or treatment.

The genetic contribution, however, is only part of the story. SEARCH recently reported that the rate of new diagnosed cases of type 1 diabetes is increasing among youth in the United States, in the first-ever estimate of incidence trends in the five-major racial/ethnic groups in the nation. The relative annual increase in the incidence of type 1 diabetes, from 2002 to 2012, was about 1.8 percent.[23] This study also found that the increase in incidence was not shared equally among racial/ethnic groups. Although historically, type 1 diabetes has been considered to affect primarily non-Hispanic white youth, the new data demonstrate that type 1 diabetes is an increasing burden for minority youth. The rate of new diagnosed cases increased most sharply in Hispanic youth, a 4.2 percent annual increase. In non-Hispanic blacks, the rate increased by 2.2 percent and in non-Hispanic whites by 1.2 percent per year. These findings generate many questions, such as why the increase in rates of type 1 diabetes development varies so greatly and is so concentrated in specific racial and ethnic groups. Further research could illuminate the factors behind these differences and provide important clues to tailoring prevention approaches.

Rising rates of type 1 diabetes suggest that there is an unknown factor—or factors—in the environment that interacts with genetic risk to trigger disease onset or protect against it. Identifying these—such as an infectious agent, dietary factors, or some other factor—is critical to understanding the disease process and to developing prevention strategies. Toward these goals, NIDDK, through the *Special Diabetes Program*, supports an ambitious, long-term clinical research study called The Environmental Determinants of Diabetes in the Young, or TEDDY. After screening over 425,000 newborns, TEDDY is currently following over 6,000 of them at high genetic risk of type 1 diabetes until they are 15 years old. Dedicated parents and researchers are regularly collecting information about the children's diet, allergies, illnesses, and other environmental exposures. Additionally, over 3.2 million biological samples have been collected to date—the most data and samples ever collected on newborns at risk for autoimmunity and type 1 diabetes. These samples are a treasure trove now being analyzed with state-of-the-art genomic, metabolomic, and proteomic technologies to uncover possible environmental triggers and protective factors. Microbiome research—to study the microorganisms that populate the digestive tract—in TEDDY is also shedding light on the broader development of the microbiome as TEDDY is one of the largest studies of the microbiome in children. TEDDY is another example of a long-term effort that could pay major dividends and give unique insight into type 1 diabetes and children's health.

[23] https://www.ncbi.nlm.nih.gov/pubmed/28402773

TESTING STRATEGIES TO STOP THE AUTOIMMUNE ATTACK AND PRESERVE BETA CELLS

As new environmental triggers are identified by TEDDY and novel insights emerge from research on the function of risk genes, NIDDK's Type 1 Diabetes TrialNet is uniquely positioned to test promising prevention strategies. TrialNet, through the *Special Diabetes Program*, supports the development and implementation of trials to test novel strategies aimed at preventing type 1 diabetes in people at risk and slowing disease progression in people newly diagnosed. These trials go hand-in-hand: not only are TrialNet and NIAID's Immune Tolerance Network studies in people newly diagnosed potentially beneficial to participants by preserving remaining beta cell function, these studies also provide critical information for prevention research. For example, after finding that the drug abatacept was safe and preserved beta cell function in people newly diagnosed with type 1 diabetes, TrialNet investigators are now studying its use for prevention in people at high risk for the disease. Building on similar findings in other successful new-onset studies, TrialNet has also launched a prevention trial with the anti-CD3 monoclonal antibody, teplizumab. TrialNet recently announced results from a third prevention study using oral insulin: the major study population did not benefit, but in a smaller group, with more advanced disease, fewer people developed a clinical diagnosis of type 1 diabetes. Ongoing studies are comparing immune responses to different doses of oral insulin, providing new key information about this agent.

The ability to assess accurately those at risk for type 1 diabetes is critical for identifying individuals in the general population, so that as many people as possible can benefit if and when new prevention strategies are proven effective. TrialNet also supports research to understand the natural history of type 1 diabetes and identify people at risk for the disease. To date, TrialNet has screened over 160,000 individuals—and screens approximately 15,000 new individuals per year—for type 1 diabetes risk to identify those eligible for participation in TrialNet prevention studies. Data from this TrialNet study, TEDDY, and other studies demonstrated that progression of type 1 diabetes proceeds through distinct stages, allowing identification of the disease before symptoms appear. This forms the basis for a new recommendation from JDRF, the Endocrine Society, and the ADA for a type 1 diabetes staging classification in at-risk individuals that provides a framework for the research and development of preventative therapies.[24] TrialNet will begin piloting use of finger sticks to collect blood for antibody screening; this could greatly increase the number of children and ease with which they are screened for type 1 diabetes. These high-risk, high-reward studies to identify, test, and—based on advances in screening—deliver these prevention strategies are poised to inform critical future public health efforts to identify those at risk and to intervene to prevent type 1 diabetes.

EMERGING OPPORTUNITIES IN TYPE 1 DIABETES RESEARCH

The advances I have discussed today are just a few examples of the exciting progress in research on type 1 diabetes and its complications. The investments we have made in infrastructure, technology, and human potential are bearing fruit. We are learning so much so

[24] https://www.ncbi.nlm.nih.gov/pubmed/26404926

quickly, and the results of this research are improving the lives of people with type 1 diabetes. But we cannot rest yet, and we cannot slow down. To capitalize on the recent research progress I described and to take advantage of advances in cutting-edge technology, NIDDK, under the auspices of the statutorily required Diabetes Mellitus Interagency Coordinating Committee, solicited input from scientific and lay experts about future research directions in type 1 diabetes and its complications at a workshop held this past April.[25] The opportunities that emerged from that workshop are extensive and exciting, such as the ability to increase understanding of the immunology of type 1 diabetes toward new prevention and cure strategies. For example, high risk for type 1 diabetes, in those with genetic susceptibility, is predicted by the presence of two or more antibodies that recognize different cellular components (autoantigens). Powerful new technologies provide opportunities to facilitate discovery and characterization of new autoantigens and the immune response to them, which could be used to monitor disease progression and response to treatment and, potentially, could lead to novel therapies. In another example, it may be possible to change the course of the disease, or to prevent it entirely, by interfering with the pathways leading to autoimmunity. Recent discoveries in the field of cancer immunology demonstrate that tumors can evolve to evade the immune system. They do this, in part, by activating the normal mechanisms by which undamaged or uninfected cells turn off immune responses after an infection. What if we could do this in type 1 diabetes? What if we could specifically and safely deactivate the "over active" immune system in type 1 diabetes? Innovative research in this area could lead to identification of compounds or development of vaccines to safely restore normal immune system functioning in people with type 1 diabetes.

The timing is also right to capitalize on advances in single-cell analysis. Many biological experiments are performed on groups of cells, assuming that all cells of a particular "type" are identical. But, we are learning that individual cells within a population may differ dramatically, and these differences can have important consequences in health and disease. Single-cell analysis promises to enhance understanding of individual cells, and we are eager to apply this to the human islet tissue environment. Detailing the identity at the cellular and molecular levels and the function of important components of islet architecture at high resolution could help to improve understanding of the early steps of the disease process toward preventative approaches, develop highly specific therapeutic strategies based on the identification of new cellular and molecular targets, and improve the design and engineering of islets for cell replacement, disease modeling, and drug discovery. These are just a few of the timely opportunities poised to accelerate discovery and development in type 1 diabetes research.

NIDDK support of type 1 diabetes research will also continue to be guided by the 2011 Diabetes Research Strategic Plan,[26] which the Institute spearheaded with broad external input, and by the input that NIDDK receives at venues such as scientific conferences and workshops. With this input, NIDDK and NIH have identified the most compelling areas of research to pursue with funds from the *Special Diabetes Program* to ensure that the *Program* continues its

[25] https://www.niddk.nih.gov/about-niddk/advisory-coordinating-committees/diabetes-mellitus-interagency-coordinating-committee/Documents/DMICC_Agenda_04262017.pdf
[26] https://www.niddk.nih.gov/about-niddk/strategic-plans-reports/Pages/advances-emerging-opportunities-in-diabetes-research.aspx

exceptional track record of supporting cutting-edge type 1 diabetes research.

NIDDK also remains committed to fostering scientific collaboration and to resource sharing to reduce duplication and maximize return on scientific research investments. We remain committed to providing access to research resources to increase understanding of type 1 diabetes and its complications. For example, NIDDK supports distribution of human islets from organ donors to researchers and ancillary studies of type 1 diabetes clinical trials. Biosamples and data from completed studies are available to the broad research community through the NIDDK Central Repositories. We also support one of our most valuable resources—young investigators—through training and career development programs to recruit and retain scientists with different areas of expertise whose talents will enhance the type 1 diabetes field.

Finally, they say that the whole is greater than the sum of its parts, and this is certainly true in type 1 diabetes research. We work together with our partners—our sister HHS agencies, academic institutions, and charitable and patient advocacy groups like JDRF, the Helmsley Charitable Trust, and ADA—and what we achieve collaboratively is changing the lives of the people with type 1 diabetes. This teamwork—like the collaboration among NIDDK, JDRF, and FDA to help advance artificial pancreas technologies—is essential and powerful, and propelled us toward the first approved hybrid artificial pancreas device, with several other promising devices in pipeline.

With the remarkable progress already achieved through support from the *Special Diabetes Program*—and the promise of future research—the goals are clear. In the near term, artificial pancreas technologies will transform the lives of people with type 1 diabetes, making blood glucose control safer and less arduous. New ways to restore and protect beta cells may yield a cure for those with the disease. Medicines that prevent life-threatening disease complications may be developed. Finding the genes and environmental factors that contribute to type 1 diabetes may produce ways to identify those at risk at birth and safely prevent the disease, thereby eliminating new cases. With continued research, it is possible to imagine that people could lead a life free of the burden of type 1 diabetes and its complications.

CONCLUDING REMARKS

I appreciate this opportunity to share with you these exciting advances, ongoing efforts, and emerging opportunities in type 1 diabetes research. We are grateful for the continued support of Congress that has allowed NIH to vigorously support research to combat type 1 diabetes and its complications. We look forward to continuing our strong partnerships with patient advocacy groups, research institutions, and our sister federal agencies. We also thank the clinical study volunteers, without whom the clinical research I described today would not be possible. Working with these partners, NIH remains steadfast in our goals of preventing, treating, and ultimately curing type 1 diabetes.

Thank you, Chairman Collins, Ranking Member Casey, and Members of the Committee for your attention. I will be pleased to answer any questions you may have.

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Director, National Institute of Diabetes and Digestive and Kidney Diseases

Dr. Griffin P. Rodgers was named director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) at the National Institutes of Health on April 1, 2007. Dr. Rodgers served as the NIDDK's acting director March 2006 - April 2007 and was the Institute's deputy director from 2001 - 2007. Since 1998, Dr. Rodgers also serves as chief of the Molecular and Clinical Hematology Branch. The branch is now administratively managed by the NIH's National Heart, Lung, and Blood Institute.

Dr. Rodgers received his undergraduate, graduate, and medical degrees from Brown University in Providence, RI. He performed his residency and chief residency in internal medicine at Barnes Hospital and the Washington University School of Medicine in St. Louis. His fellowship training in hematology/oncology was through a joint program of the NIH with George Washington University and the Washington Veterans Administration Medical Center. In addition to his medical and research training, Dr. Rodgers earned a master's degree in business administration, with a focus on the business of medicine, from Johns Hopkins University in 2005.

As a research investigator, Dr. Rodgers is widely recognized for his contributions to the development of the first effective, and now FDA-approved, therapy for sickle cell anemia. He was a principal investigator in clinical trials to develop therapy for patients with sickle cell disease. He also performed basic research that focused on understanding the molecular basis of how certain drugs induce gamma-globin gene expression. Recently, he and his collaborators have reported on a modified blood stem-cell transplant regimen that is highly effective in reversing sickle cell disease in adults and is associated with relatively low toxicity.

Dr. Rodgers has been honored for his research with numerous awards, among them the 1998 Richard and Hinda Rosenthal Foundation Award, the 2000 Arthur S. Flemming Award, the Legacy of Leadership Award in 2002, and a Mastership from the American College of Physicians in 2005. He was a 2015 finalist for The Samuel J. Heyman Service to America Medals (Sammies).

Dr. Rodgers has been an invited professor at medical schools and hospitals in France, Italy, China, Japan, and Korea. He has been honored with many named lectureships at American medical centers and as commencement speaker at many medical schools. He has published more than 200 original research articles, reviews, and book chapters; has edited four books and monographs; and holds three patents.

Dr. Rodgers served as governor to the American College of Physicians for the Department of Health and Human Services from 1994 - 1997. He is a member of the American Society of Hematology; the American Society of Clinical Investigation; the Association of American Physicians; the National Academy of Medicine (formerly the Institute of Medicine) of the National Academies of Sciences, Engineering, and Medicine; and the American Academy of Arts and Sciences. He served as chair of the Hematology Subspecialty Board and a member of the American Board of Internal Medicine Board of Directors.