Diabetes Mellitus Interagency Coordinating Committee Workshop on Research Supported by the *Special Statutory Funding Program for Type 1 Diabetes Research*

March 8, 2022
Virtual

Summary

INTRODUCTION

A panel of scientific and lay experts from across the United States, with expertise relevant to type 1 diabetes and its complications, convened virtually on March 8, 2022. The goal of the workshop was to obtain input from panel members on draft concepts for research initiatives that could be pursued with funds from the *Special Statutory Funding Program for Type 1 Diabetes Research ("Special Diabetes Program" or "*the *Program")* in Fiscal Years (FY) 2023 and 2024. Furthermore, the panel was invited to propose other ideas for new and emerging opportunities for type 1 diabetes research that could be pursued with funds from the *Special Diabetes Program*. Thus, the workshop served as one of many key sources of input to the government for informing future research directions. A summary of the workshop is presented here, including descriptions of these initiatives and highlights of the relevant panel discussions.

Background on Workshop: To inform decisions about how best to use FY 2023 *Special Diabetes Program* funds, as well as funds from a possible extension of the *Program* in FY 2024, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) convened a 21 member external panel to solicit input on future research directions. The panel consisted of 20 scientific experts that had expertise in a variety of areas, and one lay panel member who provided a patient perspective and who had broad expertise in type 1 diabetes.

Because the *Special Diabetes Program* is a trans-Department program of the U.S. Department of Health and Human Services (HHS), NIDDK initiated a call for proposals/initiatives to other Diabetes Mellitus Interagency Coordinating Committee (DMICC) member organizations for research that could be pursued in FY 2023 and/or FY 2024. Specifically, NIDDK requested proposals for new concepts for research that could advance understanding and improve outcomes of type 1 diabetes or its complications.

Thirteen proposals, submitted by two Institutes of the National Institutes of Health (NIH) as well as the Centers for Disease Control and Prevention (CDC), were presented to the panel. Written summaries including background and justification, goals and objectives, and proposed cost and duration for each of the 13 proposals were provided to the panel members prior to the workshop.

Workshop Agenda: The workshop began with an overview of the *Special Diabetes Program* given by Dr. William Cefalu, Director, Division of Diabetes, Endocrinology, and Metabolic Diseases, NIDDK, and included welcoming remarks from Dr. Griffin Rodgers, Director,

NIDDK. This was followed by comments from the lay panel member who gave a short presentation of his perspective.

For each proposal under discussion at the workshop, an NIH or CDC staff member gave a presentation to describe the concept and goals. The presentation was followed by a question-and-answer period and a panel discussion period. Three or four panel members were assigned to serve as primary discussants for each proposal and were asked to make initial comments before the floor was opened to other panel members for their questions and comments. Panel members involved in an ongoing program were asked to leave the workshop during the relevant panel discussion.

There was also a closing discussion during which panel members were asked to comment on any gaps and emerging opportunities in the overall *Special Diabetes Program* research portfolio and to suggest other new and emerging areas of research that could be pursued to advance type 1 diabetes research.

NIDDK REMARKS

Welcome

Dr. Rodgers welcomed the panelists and thanked them for taking time to attend and participate in the workshop. He thanked staff from NIH and CDC for their efforts to prepare materials for the workshop and to present the initiatives. He also extended a welcome to attendees from other Federal agencies and from the patient advocacy and professional communities. Dr. Rodgers talked about the importance of the *Special Diabetes Program*, noting that the *Program* has supported many scientific advances that have improved the lives of people living with type 1 diabetes, including the tremendous progress in developing artificial pancreas and other glucose management technologies that are helping people today. NIDDK has used the *Special Diabetes Program* funds to undertake challenges that would have been impossible to address with NIDDK's regularly appropriated funding alone. This included conducting prevention trials, which led to a recent advance by NIDDK's Type 1 Diabetes TrialNet showing, for the first time ever, that early preventive treatment could delay clinical type 1 diabetes.

Responsibly administering the *Special Diabetes Program* funds and maximizing their value are among NIDDK's highest priorities, which was why the workshop was convened to solicit input from the panel of scientific and lay experts. The *Special Diabetes Program* is slated to end at the end of FY 2023. Because of the timing required to effectively plan for and develop new initiatives, NIDDK convened this workshop to discuss how best to use current funds in FY 2023 and possible future funds in FY 2024 to support cutting-edge research on type 1 diabetes prevention, treatment, and cure. Dr. Rodgers concluded by noting that input from previous panels has been critical for informing use of the funds and that NIDDK expected that this panel will provide similarly insightful feedback.

Overview of the *Special Diabetes Program*

Dr. Cefalu thanked the panel members for participating in the workshop and provided them with an overview of the *Special Diabetes Program*.

The *Special Diabetes Program* is a trans-HHS program administered by NIDDK that began in FY 1998. The *Program* augments regularly appropriated funds that the NIH receives for diabetes research, and the funds have been distributed to multiple NIH Institutes and Centers and the CDC. The *Special Diabetes Program* funds have been used differently from regular NIH appropriations to take on broad challenges in type 1 diabetes research that could not have been addressed otherwise. The *Program* has been used to support large-scale, collaborative, high-risk, high-reward research consortia and clinical trials networks that supplement, but do not supplant, research supported with the regular appropriation. Unlike regular appropriations, the funds from the *Special Diabetes Program* are limited in time and require renewal in law.

Dr. Cefalu noted that *Program* planning is a collaborative effort with other Institutes and Centers at NIH, the CDC, and other federal agencies and has included the participation of various non-federal stakeholders, including the JDRF, the American Diabetes Association (ADA), the Endocrine Society, and the Leona M. and Harry B. Helmsley Charitable Trust. The Program is coordinated by the statutory DMICC. By fostering coordination and collaboration across federal agencies, the DMICC has played an important role in guiding the *Special Diabetes Program*.

Additionally, planning and evaluation meetings such as this workshop have been pivotal to the effective use of *Program* funds. These meetings are one way that NIDDK obtains external input on research supported by the *Special Diabetes Program*. The feedback generated by these planning meetings has been critically important for identifying gaps and emerging opportunities for type 1 diabetes research. A Diabetes Research Strategic Plan (2011), developed under the auspices of the DMICC with broad input from the scientific community, patient advocacy groups, and the public, and a recent NIDDK Strategic Plan for Research developed with broad external input, also serve as important guideposts for future research.

Dr. Cefalu provided detailed information about ongoing research supported by the *Special Diabetes Program*, to help inform the panel's discussion about the proposals being presented at the meeting as well as gaps in the research portfolio. He noted that historically, the *Special Diabetes Program* has been organized around the following six major scientific goals:

- Goal 1: Identify the Genetic and Environmental Causes of Type 1 Diabetes
- Goal 2: Prevent or Reverse Type 1 Diabetes
- Goal 3: Develop Cell Replacement Therapy
- Goal 4: Improve Type 1 Diabetes Management and Care
- Goal 5: Prevent or Reduce the Complications of Type 1 Diabetes
- Goal 6: Attract New Talent and Apply New Technologies to Research on Type 1 Diabetes

Under each goal, Dr. Cefalu presented information on the following categories of ongoing research:

- Research Programs/Consortia
- Investigator-Initiated Grants in Response to Funding Opportunity Announcements (FOAs)
- Recent FOAs for Additional Investigator-Initiated Research

Information on these ongoing efforts was presented to provide a broad overview of existing and planned research to which the panel could refer when considering the workshop's proposed initiatives.

NIDDK's The Environmental Determinants of Diabetes in the Young (TEDDY) study is the largest program under Goal 1. TEDDY is identifying environmental factors that protect against or trigger type 1 diabetes onset in genetically susceptible children. The *Special Diabetes Program* also supports research under FOAs to elucidate the discovery of the functions of the genes and variants that influence risk for type 1 diabetes.

There are several research programs/consortia under Goal 2, including:

- NIDDK's Standardization of C-peptide and HbA1c Measurements Program, which aims to improve and standardize HbA1c measurements and data interpretation across clinical systems and national harmonization programs, as well as to standardize C-peptide measurements;
- the Immune Tolerance Network, led by the National Institute of Allergy and Infectious Diseases (NIAID), which is a collaborative network for research to accelerate the clinical development of immune tolerance therapies;
- the NIDDK-led Type 1 Diabetes TrialNet, which is an international consortium that offers risk screening for relatives of people with type 1 diabetes and conducts innovative clinical studies testing ways to slow down and prevent disease progression; and
- NIDDK's new Type 1 Diabetes in Acute Pancreatitis Consortium, which aims to study the occurrence of new-onset diabetes during an episode of acute pancreatitis or subsequently, with an emphasis on type 1 diabetes.

In addition to these and other ongoing research projects, Dr. Cefalu discussed several FOAs under Goal 2, through which awards to advance type 1 diabetes prevention research may be made using current *Special Diabetes Program* funding.

NIDDK-led research programs/consortia under Goal 3 include:

- the Collaborative Islet Transplantation Registry, which compiles and analyzes islet transplantation data with the intent to capture all clinical activity in North America as well as at additional sites in other countries;
- the Integrated Islet Distribution Program, which facilitates the distribution of human islets to biomedical researchers by establishing partnerships with qualified islet isolation facilities; and
- the Human Islet Research Network, which organizes and supports collaborative research related to the loss of functional beta cell mass in type 1 diabetes.

Under Goal 4, Dr. Cefalu described how the *Special Diabetes Program* has contributed to significant progress in the development of type 1 diabetes management technologies, including artificial pancreas devices and a ready-to-use glucagon rescue pen. He also presented information about numerous FOAs that support active research grants related to improving type 1 diabetes management and care. Examples of current FOAs under which additional awards are expected to be made include an FOA for pilot and feasibility studies to improve technology adoption and reduce health disparities in type 1 diabetes, and an FOA to establish a clinical consortium to determine the factors that contribute to heterogeneity in the restoration of impaired

hypoglycemia awareness and improved counter-regulatory responses in adults with type 1 diabetes.

Under Goal 5, the National Eye Institute (NEI) leads the DRCR Retina Network to support the identification, design, and implementation of multicenter clinical research initiatives focused on retinal disorders, including diabetic retinopathy. Additionally, Dr. Cefalu noted that a previous expert panel encouraged NIDDK to use *Special Diabetes Program* funds to support research on cardiovascular disease and type 1 diabetes. Thus, NIDDK and the National Heart, Lung, and Blood Institute (NHLBI) have collaborated on new initiatives on this topic, with the first set of grants recently awarded under an FOA focused on understanding and reducing cardiovascular disease in type 1 diabetes.

In discussing Goal 6, which includes ongoing research supported by small businesses, Dr. Cefalu reminded the panelists that the same set-aside requirements regarding research conducted by small businesses that apply to the NIH regular appropriation also apply to the *Special Diabetes Program*. Dr. Cefalu asked the panel members to consider opportunities to utilize those funds. He also described several efforts related to attracting new talent to type 1 diabetes research, including ongoing career development programs for adult and pediatric endocrinologists and a program intended to provide an opportunity for new investigators/researchers to pursue their studies within the intellectual environment of a select number of large, ongoing collaborative research programs.

PATIENT PERSPECTIVE

Mr. Tom Chapman provided comments from the patient perspective. He first acknowledged the role of federal research support and the work of physicians and scientists for advancements in type 1 diabetes treatments, such as hybrid closed-loop systems. However, he also stated that type 1 diabetes is an extremely difficult disease to manage and many people do not achieve recommended blood glucose levels. Mr. Chapman noted that people with the disease face many challenges, including the risk of developing long-term complications, the psychological impact of the disease, the fear of new diagnosis in families, a fragmented healthcare system, affordability of treatments, and difficulty finding an endocrinologist. Additionally, he noted the lack of treatment options and suggested that incentives be provided to manufacturers for developing new therapies.

Mr. Chapman highlighted several important focus areas of type 1 diabetes research which have the potential to help improve clinical outcomes: (1) expand screening for type 1 diabetes (including identifying improved screening methods that do not require a blood draw), to build on the positive results of the teplizumab clinical trial for type 1 diabetes prevention; (2) build up consortia and databases to enhance collaboration and knowledge sharing across public and private entities conducting type 1 diabetes research; (3) promote psychosocial and behavioral research to study the mental burden that type 1 diabetes places on individuals and families; (4) conduct research on diabetes complications; and (5) address health disparities affecting people with type 1 diabetes.

Mr. Chapman then noted the devastating impact that the COVID-19 pandemic has had on people with type 1 diabetes. In addition to the increased risk of severe disease and death in people with

type 1 diabetes after a SARS-CoV-2 infection, the constant fear of contracting the virus has been a huge stressor for individuals and their families. However, Mr. Chapman also noted that the pandemic has created several opportunities. For example, it helped to promote the adoption (*e.g.*, by hospitals) of technologies for managing blood glucose levels and spurred the use of telemedicine as an approach to address access to care.

Mr. Chapman concluded by pondering methods for self-assessment within the research community, particularly at the federal level, inquiring as to which benchmarks and impact matrices should be considered for measuring research success. Making strategic investments of federal research dollars will lead to better patient-reported outcomes, treatments, and ultimately a cure for type 1 diabetes.

DISCUSSION OF PROPOSALS

Panel members provided input on the proposals and, in some cases, suggested enhancements. This summary includes proposals which may not be supported for a variety of reasons, may be partially supported, may be supported if contingencies are met and revisions made, may be supported through mechanisms other than the proposed Funding Opportunity Announcement (FOA), or may be supported as described.

Integrated Physiology of Exocrine and Endocrine Pancreas in Type 1 Diabetes

Primary discussants: Dr. Teresa Mastracci, Dr. Jon Odorico, Dr. James Wells

Islet destruction and dysfunction are the hallmarks of type 1 diabetes. As a result, extensive study has illuminated disease pathology primarily with respect to beta cells or islets as independent units distinct from the exocrine pancreas in which they are embedded. This focus on islet biology has, in part, contributed to a divide in the study of the pancreas between the exocrine and the endocrine compartments, with little overlap. Compelling recent evidence, however, has challenged this separation and supported the possibility of a greater interaction than previously appreciated, suggesting that a more complete understanding of the pancreas is needed to fully understand disease progression in type 1 diabetes.

The goal of this proposal is to support research aimed specifically at characterizing interactions between exocrine and endocrine pancreas. The goal of this research would be to: (1) elucidate the nature of cross-compartment interactions within the pancreas; (2) understand coordinated regulation of exocrine and endocrine tissues/cells; and (3) define mechanisms by which exocrine-derived cells and/or signaling molecules can contribute to islet function and vice versa. Advances in these areas would result in a better understanding of the relationship between exocrine function and islet biology in normal and disease states. Ultimately, identification of exocrine pancreatic regulators of islets could lead to novel target pathways in development of type 1 diabetes therapeutics.

The panel commented that this proposal addresses a compelling research opportunity that has been understudied for decades. The panel suggested expanding the benefit and reach of this program by broadening it to focus not only on interactions between the exocrine and endocrine pancreas, but to include other endocrine-mediated interactions with the beta cell that may preserve islet mass. Other panel suggestions included studying early stages of life to address

how different pancreatic cell types grow and develop together; taking advantage of new and emerging tools to examine cell-cell interactions; leveraging what is known about other forms of diabetes, including cystic fibrosis-related diabetes, to advance knowledge; examining exocrine-based neoantigens; and studying how exocrine-endocrine interactions change during checkpoint inhibitor treatment.

Human Islet Research Network (HIRN) Type 1 Diabetes Pancreas Knowledgebase Program

Primary discussants: Dr. Rong Fan, Dr. Huilin Li, Dr. Avi Ma'ayan

Solving the grand challenges in type 1 diabetes research, including how the disease is initiated, needs innovation and multi-disciplinary collaboration. As big data has become the new paradigm of biomedical research, there is an important opportunity to address this unmet need. During the past decade, the type 1 diabetes research community has generated a large amount of data by measuring the molecular and cellular events occurring at the site and around the time of initiation of beta cell destruction. To further accelerate innovation, these big data need to be leveraged using advancements in modern data science technologies, integrated with domain knowledge. However, biologists who design and conduct experiments and generate the data are often not familiar with sophisticated mathematical and computational approaches and the latest data science tools. Additionally, computational scientists who develop the tools and know how to handle data, may not have deep appreciation of the underlying biology behind the data and biological insights into how to interpret data analysis outcomes.

The goal of this proposal is to develop a type 1 diabetes pancreas knowledgebase that enables open collaboration and bridges big data to domain knowledge and advanced data science tools, to accelerate innovation and discovery toward solving grand challenges in type 1 diabetes research. The knowledgebase would be a program under HIRN, with the following components and functionalities: database, library of analytics, people (*e.g.*, projects would be driven by the type 1 diabetes research community), cyberinfrastructure technology, and partnership/collaboration.

The panel commented that this type of program is critically needed for type 1 diabetes research and is distinct from existing platforms. The panel suggested that applicants to the program be encouraged to propose technologies that are forward looking, to avoid having data that would soon be obsolete or provide limited knowledge. They also stressed the importance of testing computational predictions; emphasizing outreach and training to engage the type 1 diabetes research community; and incorporating metrics of success to ensure that the knowledgebase is attracting users. Building a social network would also be critical to bring together experimentalists and computational experts. The panel suggested providing funds in the grant budget to foster collaborations between the knowledgebase team and type 1 diabetes researchers.

Human Islet Research Network-Consortium on Modeling of Autoimmune Diabetes (HIRN-CMAD) (HIRN-CMAI/CHIB Phase III)

Primary discussants: Dr. Rong Fan, Dr. Matthias von Herrath, Dr. James Wells

The HIRN-Consortium on Modeling Autoimmune Interactions (CMAI) and the HIRN-Consortium on Human Islet Biomimetics (CHIB) are two of the four founding HIRN consortia that began in 2014. Their goals were to develop humanized *in vivo* models to

interrogate the cellular interactions leading to type 1 diabetes autoimmunity (HIRN-CMAI), and to develop human microphysiological systems (MPS)/organs on a chip for *in vitro* modeling of disease pathophysiology, including interactions between islet cells and components of the immune system (HIRN-CHIB). Given progress made by both consortia, NIDDK proposes a convergence of efforts where both HIRN-CMAI and HIRN-CHIB MPS-based models would be integrated into a novel type 1 diabetes translational research strategy bridging basic, pre-clinical, and clinical research. An expansion of investigations focused on complementary efforts in research methods and strategies is now needed to coordinate the development of both *in vitro* and *in vivo* models. It is anticipated that the development of these new/advanced models will contribute to a better understanding of the etiology/pathogenesis of type 1 diabetes, uncover mechanisms underlying diabetes heterogeneity, and ultimately point toward new avenues for development of targeted therapies. Unifying these two consortia into one may effectively promote and expedite further research in the field and attract new research talent able to design and apply innovative approaches and technologies to preclinical translation for type 1 diabetes.

The goal of this proposal is to consolidate activities pursued within the HIRN-CMAI and HIRN-CHIB into a new consortium designed to support further development and validation of *in vivo* and *in vitro* models of immune-mediated diabetes in what would represent a third period of funding. The aims of the newly formed HIRN-CMAD would be to develop approaches and systems that enable studies of human pathophysiology of diabetes and that provide platforms for pre-clinical assessments of new interventions for human type 1 diabetes.

The panel commented that this was an excellent time to undertake this area of research and merge the two existing HIRN consortia—there is already a strong foundation based on knowledge about human type 1 diabetes pathogenesis and there is no longer a distinct separation between *in vivo* and *in vitro* models. The panel noted that the models do not need to be perfect to be useful, and suggested using informative tools (*e.g.*, genome-wide mapping) to characterize the models. The panel also suggested expanding the cell types and factors studied in the islet niche, which could help to address important unanswered questions such as whether chronic inflammation associated with obesity plays a role in increased rates of type 1 diabetes. As such, different models may be needed to address various key questions in type 1 diabetes research.

Clinical, Behavioral, and Physiological Studies of Open- and Closed-loop Platforms: Toward Personalized, Fully Automated, Accessible Systems (reissue)
Primary discussants: Dr. Sue Brown, Dr. David Maahs, Dr. Paul Wadwa

Emerging and next-generation technologies for managing type 1 diabetes require pilot and transitional studies to evaluate their safety, accuracy, and efficacy as research progresses from animal and simulated models to advanced and pivotal real-world studies in people with type 1 diabetes. This research aims to optimize operability, taking into consideration patient preferences and behavioral and physiological factors, to achieve the goal of viable, functionally integrated open- and closed-loop systems for routine use. It is also critical to test these technologies in people usually not included in clinical trials (*e.g.,* groups who are underserved or marginalized, people who are pregnant) and/or considered high-risk (*e.g.*, people with high HbA1c, frequent severe hypoglycemia, hypoglycemia unawareness, high glycemic

variability/lability, recently diagnosed, tendency to develop diabetic ketoacidosis, autonomic neuropathy) who may be the ones with the greatest need for these advanced interventions.

The goal of this proposal is to support research for the initial testing of emerging open- and closed-loop hormone delivery systems, addressing barriers that limit their usability and accessibility. Specifically, the initiative would support research to: (1) test and improve the accuracy, safety, reliability, and usability of these technologies in humans; (2) test emerging approaches for better integration and interoperability of components; (3) address behavioral and psychosocial factors and outcomes; and (4) advance understanding of pathophysiology and metabolic regulation in people with type 1 diabetes.

The panel commented that this is a critical area of research that has had many important advances as a result of *Special Diabetes Program* and NIDDK support. Even with this success, research is needed to ensure that all people with type 1 diabetes can benefit from these advances and new technologies, and panelists noted that this proposal can accelerate such research. A panel member noted that, although people using these technologies have improved their glycemic outcomes, many are still not meeting optimal glycemic targets. Therefore, understanding the behavioral barriers to adoption and use of these technologies is needed, as is developing implementation strategies to support the adoption and uptake of the research findings into policy and practice to make these technologies more accessible. Many panel members noted concern about the potential for increasing disparities if these technologies are too expensive, difficult to attain, or difficult to use. A panel member emphasized the importance of telemedicine in this area and suggested that synergies with other proposals focusing on social and healthcare interventions to reduce disparities may be fruitful. Finally, the discussants echoed the importance of the proposed plans to include populations usually not included in clinical trials, such as women who are pregnant, people who are underserved, and the very young.

Studies to Develop and Adapt Diabetes Technologies for Older Adults with Type 1 Diabetes
Primary discussants: Dr. Sue Brown, Dr. David Maahs, Dr. Paul Wadwa

Older adults with type 1 diabetes have significantly higher rates of severe hypoglycemia compared to younger adults, and over half of this population spend at least an hour a day with glucose levels in the hypoglycemic range (< 70 mg/dL). The consequences of hypoglycemia include increased morbidity, seizures, cognitive impairment, hypoglycemia unawareness, visits to the emergency room, and mortality. Studies suggest that use of diabetes technologies in independent older adults can decrease hypoglycemia and improve time-in-range, but many older adults with diabetes have impairments in independent activities of daily living and need assistance using these technologies. Additionally, there are many social and institutional barriers in using these technologies for caregivers of older adults with type 1 diabetes. There is a need for diabetes technologies that can adapt to age-related changes in cognition, vision, hearing, manual dexterity, and different living and care situations so that older adults with type 1 diabetes can continue to use these technologies and their caregivers can provide support.

The goal of this proposal is to foster the development, adaptation, and testing of new or existing diabetes technologies in older adults with type 1 diabetes to reduce hypoglycemia and hypoglycemia unawareness, improve glycemic control and management, and enhance quality of

life. Pilot trials would test adapted existing technologies and engage stakeholders (*e.g.*, patients, caregivers, healthcare providers, and staff) to assess the barriers and facilitators to adoption and use of technology and to test strategies to overcome these barriers. Additional research projects would support the development and testing of new technologies.

Panel members thought this was an important area of research and supported the proposed requirement for stakeholder engagement in the pilot studies. One panel member commented how important it is to understand the perspectives of the different stakeholders—the person with diabetes, their family, the physician(s) providing care, caregiving facilities—to determine how they can be better supported in caring for an individual with diabetes. Panel members also noted that, in creating opportunities for structured input from stakeholders, the research outcomes may be more easily disseminated to create and provide education for caregivers, especially in situations where the person with diabetes may no longer be independent or in situations of "therapeutic inertia" where providers may have hesitancy in promoting new technologies. Another panelist commented how important an easy-to-use user interface will be for this population and that improving existing technology could have significant benefits for older people with diabetes. Panelists suggested expanding this research to include other groups for whom the technologies are underutilized and in whom there are opportunities to improve clinical outcomes, including racial and ethnic minority groups and the very young.

Stakeholder Engagement Innovation Center

Primary discussants: Dr. Monica Baskin, Dr. Bill Herman, Dr. David Maahs, Dr. Monica Peek

A fundamental approach for tackling health disparities and promoting equity involves meaningful stakeholder engagement with individuals and communities that are 'hardly reached' to understand their lived experiences and values and improve clinical research outcomes in type 1 diabetes. Although groups who are underserved or socially and economically disadvantaged tend to have poorer type 1 diabetes outcomes, their participation and voices are often lacking in type 1 diabetes research. Stakeholder engagement that involves trust building, use of culturally appropriate research designs, questions, and materials (*i.e.*, outreach, recruitment, informed consent documents) is an important method to enhance and assess research outcomes including participation goals, health specific outcomes, and sustainability. Although engagement activities with the community may require additional research time, the opportunity to promote health equity and reduce disparities far outweighs this potential challenge. Investigators, however, often lack expertise in stakeholder engaged methodologies, so strategic investments in the type 1 diabetes community are required to facilitate and promote meaningful stakeholder engagement.

The goal of this proposal is to establish a novel national Stakeholder Engagement Innovation Center to enhance meaningful stakeholder participation and involvement in clinical studies, improve recruitment and retention, use community-driven and community-engaged methods and approaches, and improve health equity in type 1 diabetes. The Center would provide research resources such as expert engagement teams, individual consultations, and education in conducting stakeholder and community-engaged research, and develop a community of diverse, multidisciplinary researchers with expertise in critically needed methods.

Panel members commented on the importance of stakeholder engagement, noting that this proposal could have an impact across research areas and synergize with other NIDDK programs such as the Diabetes Translation Research Centers and career development/training programs. Panelists emphasized that thoughtful community engagement needs to be done with the communities and expertise local to the study sites; thus, it is important for investigators to learn from the Innovation Center how to reach out and interact with their own local communities. A panelist also encouraged support of research teams that included community partners and people with type 1 diabetes in the design and conduct of the research. Another suggestion was for the Innovation Center to have a broader impact on the research community by sharing lessons learned and developing resources that could be disseminated to help other investigators with meaningful stakeholder engagement. Several panelists cautioned that, while there would be clear benefits in terms of increasing diversity of research participants and community input, this program would need to be complemented by more focused efforts to advance health equity and reduce disparities, including a larger health equity framework around the impact of behavioral barriers, social determinants of health, access to care, financial barriers, and issues related to training and decision support in type 1 diabetes care.

Integration of Social and Medical Care Interventions for Type 1 Diabetes
Primary discussants: Dr. Monica Baskin, Dr. Bill Herman, Dr. David Maahs, Dr. Monica Peek

The social determinants of health (SDoH)—the conditions in which people live, work, play, and pray—have a significant role in determining health outcomes and thus need to be addressed. SDoH disproportionately affect individuals of racial and ethnic minority populations who are economically disadvantaged, and contribute to avoidable, unsustainable healthcare costs in the United States. Opportunities exist to improve person-centered medical care and population health, such as raising awareness of social risk to modify clinical care or providing social assistance, and there is opportunity within the growing healthcare system IT infrastructure to support collecting and sharing SDoH data. For example, across the country, there is growing use of electronic medical record applications to collect SDoH data during clinical encounters, yet there is an absence of robust evidence for optimal strategies on the collection of SDoH data and subsequent actions to take after the collection.

The goals of this proposal are to promote health equity and address disparities with novel research on systemically screening and addressing social risks of people with type 1 diabetes; grow a community of diverse NIDDK researchers with expertise in strategies to integrate social-medical care in the context of healthcare delivery; and attract investigators and organizations with unique perspectives to broaden research on the social needs for optimal care of people with type 1 diabetes. These would be achieved through pilot and feasibility trials designed to collect preliminary evidence on the feasibility of systematically screening for SDoH at the point-of-care, making appropriate referrals/navigation to services that address health-related social needs/risks endorsed by people with type 1 diabetes (or their families or caregivers, as appropriate), and measuring the impact on health outcomes in people with type 1 diabetes.

A panel member noted that, given how consequential SDoH are to health outcomes, this research is needed. Another panel member commented that many of the populations that would be

studied to advance health equity may not have the community resources critical to the success of this type of research, thus it would be key that a service-providing partner be identified either before the application or early in the development stage to build a strong relationship. Relatedly, NIDDK may consider collaborating with federal partners such as the Department of Agriculture, Department of Housing and Urban Development, and Department of Transportation. Another panel member commented that the infrastructure costs could be a huge barrier, especially to fund diabetes management technologies. Other suggestions included building cost-effectiveness analyses into the studies to demonstrate that interventions could be sustainable; bringing implementation scientists more formally into this research to grow a cadre of these scientists with expertise in type 1 diabetes and SDoH to address several of the proposals presented at the workshop; and using the T1D Exchange as a model for combining data collection and implementing studies in the type 1 diabetes population.

Precision Medicine for Type 1 Diabetes Nephropathy

Primary discussants: Dr. Karin Bornfeldt, Dr. Bill Herman, Dr. Annemarie Hirsch, Dr. Anette-Gabriele Ziegler

Approximately one-third of people with type 1 diabetes develop kidney dysfunction, which frequently progresses to end-stage kidney disease requiring hemodialysis or a kidney transplant for survival. Unfortunately, progress in treating diabetic kidney disease over the last 20 years remains limited, notably in those with type 1 diabetes, as the use of SGLT2 inhibitors remains contraindicated. Accordingly, better understanding of the pathophysiologic processes leading to progressive diabetic kidney disease is urgently needed to discover novel targets for treatment beyond glycemic and blood pressure control and to implement personalized treatment strategies. Application and integration of "multi-omics"-based approaches with properly matched longitudinal cohorts are needed to shed further light on the underlying molecular processes that lead to poor outcomes, and facilitate the identification of novel therapeutic targets.

The goal of this proposal is to leverage the participants, network of investigators and centers, and extensive resources from the completed Preventing Early Renal Loss in diabetes (PERL) clinical trial of allopurinol treatment in individuals with type 1 diabetes-associated diabetic kidney disease and the ongoing Kidney Precision Medicine Project (KPMP) to study, in depth, the clinical and molecular determinants of diabetic kidney disease progression and associated clinical outcomes. This new effort would be well poised to develop a deep understanding of the complex interacting processes leading to the progression of type 1 diabetes nephropathy and associated outcomes through: (1) identification of clinical factors associated with long-term outcomes; (2) identification of novel prognostic biomarkers; and (3) delineation of the varied underlying molecular pathophysiologic processes and novel diseases sub-types. Such knowledge could lead to methods to allow accurate assessment of individual-level risk and disease state and to develop needed targeted therapies.

Panel members expressed interest in pursuing diabetic kidney disease research and commented on the importance of adding new participants as well as other racial and ethnic populations to diversify the PERL cohort so that outcomes are more representative and generalizable. They also suggested adding some clinical measures. One panel member suggested there would be more value in enriching the diversity of the population with type 1 diabetes of KPMP

participants, while another noted the value in having such a well characterized longitudinal cohort of PERL to continue this research. Finally, a panelist encouraged collaborations with research on other type 1 diabetes complications to maximize investments.

Risk Mitigation Strategies for the Use of Sodium-Glucose Co-transporter-2 Inhibitors (SGLT2i) in Type 1 Diabetes

Primary discussants: Dr. Alessandro Doria, Dr. Bill Herman, Dr. Rodica Pop-Busui, Dr. Anette-Gabriele Ziegler

Sodium-glucose co-transporter-2 inhibitors (SGLT2i) are a new class of anti-glycemic agents developed to treat type 2 diabetes by inhibiting glucose reabsorption in the kidney. In addition to their glucose-lowering effect, they have been found in several Phase III trials to decrease all-cause mortality, cardiovascular events, heart failure hospitalization, and renal disease progression, with remarkable reductions in hazard ratios of 0.85, 0.91, 0.7, and 0.61 respectively, in people with and without type 2 diabetes. However, the benefits of these morbidity- and mortality-reducing drugs are not being shared with the type 1 diabetes community, as the risk of diabetic ketoacidosis (DKA) is increased ~3-fold with their use. Given the overwhelming benefits of these drugs, in a wide range of individuals, they have still been approved for use in people with type 1 diabetes in some countries and are being used "off-label" for that purpose in the United States. To reduce the risk of DKA associated with this therapy, several groups have published guidelines related to patient selection and monitoring for DKA. Unfortunately, these guidelines are not evidence-based and have not been systematically evaluated or tested. In addition, developments in continuous ketone monitoring could lead to better assessment of risk and incorporation in risk mitigation strategies. As such, there is an urgent need to better understand risk factors and predictors for DKA to allow for mitigation strategies to ensure the lowest risk feasible in high-risk individuals with type 1 diabetes who are expected, as in individuals with and without type 2 diabetes, to significantly benefit from SGLT2i use.

The goal of this proposal is to develop and test risk mitigation strategies for life-threatening DKA in individuals with type 1 diabetes-associated cardio-renal disease who are expected to benefit from SGLT2i use. This research would provide needed evidence to understand the correlates of SGLT2i-related DKA and to test validity and feasibility of potential risk mitigation strategies.

Many panel members commented that this proposal covered an important topic of concern to the type 1 diabetes community. Several panel members felt that the proposed studies could facilitate expansion of the currently limited pharmacological tools available specifically to help people with type 1 diabetes. One panel member pointed out that SGLT2i medications are one of few treatment options that address the cardiovascular complications of diabetes, and that wariness about DKA can prevent their use by those with type 1 diabetes. Several panel members emphasized the importance of using good proxies for predicting and measuring DKA in the proposed studies, and also suggested reviewing data from previous observational datasets and/or registration trials to design the proposed research. Additionally, the panel noted that engaging with industry for these studies would be beneficial, both to benefit from industry expertise and perhaps to help with cost-sharing. One panel member pointed out that studying risk mitigation strategies alone before an agent is approved for use may be premature. Several panel members

also suggested expanding the proposed studies to investigate efficacy side by side with risk mitigation strategies, to move the field forward more quickly.

Early Complications Among Individuals with Incident Type 1 Diabetes
Primary discussants: Dr. Gillian Booth, Dr. Alessandro Doria, Dr. Anette-Gabriele Ziegler

Among adults, multifaceted improvements in diabetes care, risk factor management, self-management support, and better integration of care reduced the risk of macro- and microvascular complications by 28 to 68 percent between 1990 and 2010. Reductions were largest for incident acute myocardial infarction, stroke, and death due to hyperglycemia over this period. An updated analysis of trends in diabetes complications using the same databases, however, indicated an increase in diabetes-related lower extremity amputations, hyperglycemic crises, and annual emergency department visits after 2010, reversing the previous 20-year decline seen nationally. For incidence of end-stage kidney disease, acute myocardial infarction, and stroke, previous favorable trends stalled after 2010. These recent trends in the risk of diabetes complications were particularly evident in young and middle-aged adults. National databases (*e.g.*, National Health and Nutrition Examination Survey [NHANES], National Health Interview Survey [NHIS]) offer insufficient granularity to further explore the reasons and determinants for these recent trends. The Diabetes in Children, Adolescents, and Young Adults (DiCAYA) study, supported by CDC and NIDDK, includes this type of information but currently lacks the follow-up time to explore risks and trends in type 1 diabetes complications and how these differ from those seen in type 2 diabetes.

The goal of this proposal is to support research to measure risk of and trends in type 1 diabetes complications and the social, environmental, and clinical attributes associated with their onset and progression. The initiative would establish a racially and ethnically diverse cohort of newly diagnosed individuals ages 0-45 years with type 1 or type 2 diabetes, as identified by the DiCAYA study. Specifically, the initiative aims to follow a relevant subset of the DiCAYA cohort with incident type 1 and type 2 diabetes. This follow-up would help to understand the clinical course of youth- and young adulthood-onset diabetes—including the incidence of acute and chronic complications—as well as the social, environmental, and clinical attributes associated with diabetes onset and progression.

The panel noted that this proposal offers an opportunity to provide needed information on the prevalence of diabetes and diabetes complications. Several panelists commented that this proposal was a unique opportunity to build upon the extensive and unique DiCAYA study but raised concerns that the proposed 5-year follow-up might not be long enough to observe long-term complications in those with new-onset type 1 diabetes. To truly examine the incidence of long-term complications, panelists suggested that a much longer study would be needed and/or the study might need to focus on those who had type 1 diabetes for a longer duration. Despite these concerns, panelists also recognized that this proposal could build the necessary framework for such a longer study. One panel member suggested that information gained from previous studies could be used to enrich the study population for those at risk for early complications. Another suggestion was for the proposed study to include biosamples from participants to facilitate identification of biomarkers. Another concern raised by one of the panel members was that following young adults through electronic health records (as in DiCAYA) might be difficult,

as this population moves around, would make retention difficult and individuals can lose insurance.

Efficacy and Implementation of Cardiovascular Risk Reduction in Type 1 Diabetes Mellitus

Primary discussants: Dr. Karin Bornfeldt, Dr. David Maahs, Dr. Rodica Pop-Busui

Epidemiological data show that people with type 1 diabetes have shorter lifespans than the general population, which is primarily attributable to premature atherosclerotic cardiovascular disease (CVD); more than 70 percent of men and 50 percent of women with type 1 diabetes have developed coronary artery calcification by the age of 45. Because type 1 diabetes typically occurs in youth, many individuals have evidence of significant clinical CVD risk factors (*e.g.*, elevated blood pressure, dyslipidemia, obesity) by adolescence and young adulthood. Accelerated atherosclerosis in type 1 diabetes is thought to result from many pathways including effects from inflammation, dyslipidemia, hypertension, and nephropathy, whereby these known risk factors may operate differently in type 2 diabetes, suggesting a difference in the pathophysiology of CVD. Data about the appropriate timing of initiation of hypertension and dyslipidemia treatment in individuals with type 1 diabetes are limited. Several newer agents have emerged with renal and/or cardiovascular benefits (*e.g.*, SGLT2i, glucagon-like peptide-1 receptor agonists [GLP-1 RA]) among individuals with type 1 diabetes and in some cases people without diabetes. However, people with type 1 diabetes were excluded from the relevant clinical trials and currently are excluded from the regulatory approvals for these agents. These drug classes may improve cardiorenal health in people with type 1 diabetes as they do in type 2 diabetes, but trials in people with type 1 diabetes collecting the relevant cardiovascular and renal clinical outcomes have yet to be done.

The goal of this proposal is to support efficacy and effectiveness clinical trial(s) focused on the best behavioral (*e.g.*, dietary, physical activity) and/or pharmacologic approach to CVD prevention among participants with type 1 diabetes to create a meaningful change in multiple risk factors. There is interest in understanding the individual and combined impact of both well-established and novel classes of medications at varying levels of intensity with or without aggressive lifestyle modification. This approach may require vanguard studies ahead of a larger trial. This proposal would provide an interesting opportunity to investigate how similar diabetes-related CVD is to traditional coronary artery disease versus some unique diabetes-related vascular disease.

One panelist commented on the importance of determining when and how to treat young people with type 1 diabetes to prevent cardiovascular complications, confirming that doctors can be reluctant to initiate such treatment for children given concerns about lifetime cost and possible side effects. Several panelists stated that the 7-year length of the proposed awards was a strength, given the long timeframes over which CVD can develop. One panelist pointed out that this proposal would also be an opportunity to identify what drives the differing risk of cardiovascular complications between males and females with type 1 diabetes, which could inform personalized risk-reduction strategies. Other suggestions included: studying stroke in type 1 diabetes, which is an understudied area; studying the interactions between CVD, COVID-19, and type 1 diabetes; partnering with industry to explore adding a type 1 diabetes arm to a

cardiovascular prevention trial that would otherwise exclude those with the disease; and studying the kidney's role in CVD in type 1 diabetes, perhaps by combining the measurement of kidney and heart outcomes in the proposed research.

Understanding the Role of Sleep Deficiency in Persons with Type 1 Diabetes: Sleep, Glycemic Control, and Cardiometabolic Risk

Primary discussants: Dr. Bill Herman, Dr. Rodica Pop-Busui, Dr. Maria Redondo, Dr. Paul Wadwa

Sleep deficiency (*i.e.*, insufficient sleep duration, poor sleep quality, irregular timing of sleep) and sleep disorders (*e.g.*, sleep apnea) are linked to metabolic dysregulation, including insulin resistance, impaired glucose tolerance, increased energy intake, weight gain, autonomic nervous system activation, and related cardiovascular conditions. The evidence indicates that sleep deficiency is prevalent in people with type 1 diabetes across all ages and that this population encounters unique barriers to sufficient sleep. Studies point to the mediating effects of sleep and circadian rhythms on cellular mechanisms of glucose metabolism, insulin production and release, cellular stress (*e.g.*, protein misfolding, oxidative stress), systemic inflammation, autophagy, and cytotoxicity. Together, these findings indicate that sleep deficiency may exacerbate type 1 diabetes severity, accelerate disease time course, contribute to variability in treatment response, and/or exacerbate associated risk of cardiovascular disease.

The goal of this proposal is to promote mechanistic and clinical research investigating the connections between sleep deficiency and type 1 diabetes, as well as the consequences and influences of sleep on clinical course and treatment outcomes in this population. Research opportunities include: (1) elucidating mechanisms mediating the interactions between sleep, glycemic control, and associated cardiovascular disease pathophysiology; (2) identifying sleep and circadian alterations in type 1 diabetes that contribute to variability in treatment response; and (3) determining if therapeutic sleep/circadian interventions ameliorate abnormalities in glycemic control, improve type 1 diabetes treatment outcomes, and/or reduce related cardiovascular complications. Clinical implications and findings regarding sleep as an essential component of diabetes care would improve the understanding, diagnosis, prevention, and/or treatment of type 1 diabetes, with the potential to impact clinical practice and public health.

Panelists commented that this proposal addressed a compelling and possibly high-yield scientific opportunity. Several panelists commended the proposal's focus on understanding the mechanisms behind sleep deficiency's effects, including investigating connections to social determinants of health, as well as its focus on opportunities for trainees and interdisciplinary teams to take part in the research. Another panelist noted that the proposed research could gather data to allow researchers to investigate the possible different effects of various sleep disorders (*e.g.*, sleep apnea) to other sleep disturbances such as distress over lack of sleep, alarms from glucose management devices, and/or fear of hypoglycemia. Another panelist noted that this proposal is an opportunity to look at type 1 diabetes' effects on sleep across the lifespan. Panelists also suggested that the proposed research also investigate the role of other factors (such as obesity) on type 1 diabetes and sleep deficiency. Several panelists noted that the proposal's topic was timely, as the technologies available—such as continuous glucose monitors and

wearables that can measure oxygen levels and sleep duration—are mature enough to gather a wealth of useful study data with off-the-shelf equipment.

Project Proposals for Use of The Human Type 1 Diabetes Cardiovascular Tissue Biorepository

Primary discussants: Dr. Karin Bornfeldt, Dr. Alessandro Doria, Dr. Rong Fan

Cardiovascular complications are the leading cause of death for individuals with type 1 diabetes and significantly shorten their lives. Cardiovascular disease (CVD) progression in people with type 1 diabetes differs from that observed in people with type 2 diabetes in that: (1) the former are younger at age of disease onset, and (2) a disproportionately greater effect is observed in women. Treatment of standard risk factors, such as hyperglycemia, hypertension, and hyperlipidemia, mitigates some of the higher CVD risk, but residual increased CVD risk remains even with standard-of-care. In addition to atherosclerotic disease, both diastolic and systolic diabetic cardiomyopathies are associated with significant morbidity and mortality and have complex pathophysiologic mechanisms that are not fully understood. The risk of heart failure is also significantly higher in people with type 1 diabetes compared to type 2 diabetes. However, the pathophysiology of atherosclerosis, cardiomyopathy, endothelial function, and cardiac autonomic neuropathy in type 1 diabetes is poorly understood, and no therapies are approved to prevent or treat these common, deadly complications of type 1 diabetes. Research challenges in studying CVD in people with type 1 diabetes include CVD's silent development over decades of metabolic dysregulation and the lack of preclinical models that replicate the human disease.

The goal of this proposal is to solicit and fund proposals to use samples and data from the Human Type 1 Diabetes Cardiovascular Biorepository. The awarded grantees from this proposed initiative would form a consortium to study the development of CVD in type 1 diabetes by using multimodal approaches to achieve a systematic, comprehensive, unbiased, and standardized deep phenotyping of human type 1 diabetes cardiovascular tissue. The Biorepository—which will obtain cardiovascular tissue from organ donors with type 1 diabetes, type 2 diabetes, and without diabetes—would serve as the Data Coordinating Center for the consortium. This proposed consortium would increase our understanding of type 1 diabetes-related CVD and lead to biomarker identification for early detection as well as treatments specific for those with type 1 diabetes.

One panelist mentioned that "omics" and bioinformatics scientists would be excited by the opportunity to access this biorepository, but cautioned that tissue preparation strategies would limit what downstream techniques and experiments could be done on what samples. Another panelist added that the proposed consortium structure would be an effective way to promote collaboration among the awardees. The panel also stated that having access to multiple tissues from one donor would facilitate more comprehensive studies. One panelist raised concerns about possible limitations of the biorepository, including the number of biosamples being small and a possible bias towards donors with comorbidities; sufficiently granular clinical data would need to be archived with the biosamples to allow researchers to make informed choices about sample use. Other panelists commented that managing the biosamples' metadata would be key to ensuring that relevant clinical data was considered when performing analyses. One panelist noted that lessons on metadata management could be incorporated from other consortia (such as

the Human BioMolecular Atlas Program [HuBMAP]) that manage similar collections. Another suggestion for how to obtain biosamples with well-documented clinical data attached was to pre-emptively request permission for organ donations from existing, well-characterized cohorts of people with type 1 diabetes (such as those participating in an existing study). It was also mentioned that this proposal offers an opportunity to investigate new ways to use clinically accessible tissues as surrogates to monitor the health of less-accessible tissues (such as the heart).

ADDITIONAL DISCUSSION

The expert panel made closing comments on the proposals. Specific input on proposals has been included in relevant sections above; other comments included:

- Promote synergies across proposals: The panel noted that there may be ways to integrate/coordinate research described under the proposals, as many of them have commonalities.
- Promote stakeholder participation: The panel commended the inclusion of stakeholder participation in many of the proposals. They encouraged continued and expanded stakeholder participation, given its importance in both the research process and in helping to ensure that research results are used by the people they could benefit.
- Include research on alloimmunity: The panel suggested that alloimmunity also be addressed in proposals studying autoimmunity.

The expert panel also identified promising topic areas in type 1 diabetes research that were not addressed in the proposals presented at the workshop. Fostering research in these areas could accelerate progress on the understanding, prevention, and treatment of type 1 diabetes and its complications. Areas of opportunity identified by the panel included:

- Advance dissemination and implementation of research findings: Panel members emphasized the need for dissemination and implementation research to make certain that promising type 1 diabetes research results reach all populations who could benefit from them, including racial and ethnic minority groups, persons who are underserved, and young children. For example, there is lower uptake of new diabetes management technologies in some populations (*e.g.*, racial and ethnic minority groups), so addressing barriers to promote adoption of technologies could improve health outcomes. The panel felt that conducting dissemination and implementation research is critical to advancing health equity.
- Use telemedicine approaches to reach vulnerable populations: Although telemedicine has long been available, its use has greatly increased during the COVID-19 pandemic. This development provides a new research opportunity to examine how best to use telemedicine approaches to improve health outcomes in vulnerable populations that have historically been challenging to reach.
- Screen the general population for type 1 diabetes risk: Building on the success of Type 1 Diabetes TrialNet's teplizumab clinical trial for type 1 diabetes prevention, some panel members felt it is appropriate to consider how best to screen the general population for type 1 diabetes risk to help maximize the public benefit from a future prevention therapeutic.
- Examine how obesity and the mechanisms of type 2 diabetes might influence type 1 diabetes pathology: The panel commented that the increasing incidence of type 2 diabetes and obesity highlights an urgent need to understand how type 2 diabetes risk factors (*e.g.*,

obesity and insulin resistance) affect type 1 diabetes incidence, progression, and complications. Thus, future research could delve deeper into how traditional type 2 diabetes risk factors and molecular mechanisms affect the course of type 1 diabetes, to help inform treatment strategies. One suggestion was to enhance collaboration between type 1 diabetes and type 2 diabetes research efforts across different funding entities.

- Collect and analyze real-world data: The panel articulated the need to collect and analyze real-world clinical data on type 1 diabetes to help inform future research directions.
- Support and consolidate interventional trials for diabetes complications: Research opportunities exist to support interventional trials on diabetes complications, particularly for therapies that are approved for those with type 2 diabetes but that industry is not pursuing for approval in people with type 1 diabetes. Additionally, the panel suggested including renal outcomes in trials focused on cardiovascular disease, and using new and emerging data from other research studies to identify ways to make complications trials more efficient (*e.g.*, identifying people with type 1 diabetes who are most likely to benefit from an intervention).
- Pursue studies on diabetic neuropathy: The panel noted the importance of studying diabetic neuropathy, particularly considering emerging evidence linking neuropathy with central nervous system complications and declines in cognition. This worrisome link could have a direct effect on people's ability to use diabetes management technologies.
- Utilize electronic health record (EHR) data: The panel suggested pursuing additional ways to leverage EHR data—a rich information source that is currently underutilized in type 1 diabetes research.
- Assess factors associated with research success: The panel suggested examining past research initiatives to determine factors that contribute to success. Such knowledge could help to inform future *Special Diabetes Program*-supported initiatives.
- Pursue research on gene editing technologies: The panel noted the promise of genome editing technologies to make better, fitter, and less immunogenic beta cells.

APPENDIX 1: PANEL MEMBERS

Opportunities for Research Supported by the *Special Statutory Funding Program for Type 1 Diabetes Research*: A Workshop of the DMICC
March 8, 2022

EXPERT PANEL MEMBERS

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APPENDIX 2: ACRONYMS

ADA	American Diabetes Association
CDC	Centers for Disease Control and Prevention
CVD	cardiovascular disease
DKA	diabetic ketoacidosis
DiCAYA	Diabetes in Children, Adolescents, and Young Adults
DMICC	Diabetes Mellitus Interagency Coordinating Committee
EHR	electronic health record
FOA	Funding Opportunity Announcement
FY	fiscal year
GLP-1 RA	glucagon-like peptide-1 receptor agonists
HHS	U.S. Department of Health and Human Services
HIRN	Human Islet Research Network
HIRN-CHIB	Human Islet Research Network-Consortium on Human Islet Biomimetics
HIRN-CMAI	Human Islet Research Network-Consortium on Modeling Autoimmune Interactions
HIRN-CMAD	Human Islet Research Network-Consortium on Modeling of Autoimmune Diabetes
HuBMAP	Human BioMolecular Atlas Program
KPMP	Kidney Precision Medicine Project
MPS	microphysiological systems
NEI	National Eye Institute
NHANES	National Health and Nutrition Examination Survey
NHIS	National Health Interview Survey
NHLBI	National Heart, Lung, and Blood Institute
NIAID	National Institute of Allergy and Infectious Diseases
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIH	National Institutes of Health
PERL	Preventing Early Renal Loss in diabetes study
SDoH	social determinants of health
SGLT2i	sodium-glucose cotransporter-2 inhibitors
TEDDY	The Environmental Determinants of Diabetes in the Young