226th NIDDK Advisory Council Meeting
Division of Diabetes and Endocrinology and Metabolic Diseases (DDEMD)
Sub-committee Meeting – Open Session
September 11, 2024

Attendees

DDEMD Sub-committee Members: Dr. David D'Alessio, Dr. Carmella Evans-Molina, Dr. Philipp Scherer, Dr. Elizabeth Seaquist

DDEMD Staff Members: Dr. Kristin Abraham, Dr. Beena Akolkar, Dr. Guillermo Arreaza-Rubin, Dr. Raj Basu, Dr. Olivier Blondel, Dr. Miranda Broadney, Dr. Art Castle, Dr. William Cefalu, Dr. Maureen Monaghan Center, Dr. Shavon Artis Dickerson, Dr. Thomas Eggerman, Dr. Minnjuan Floyd, Dr. Rafael Gorospe, Mr. Neal Green, Dr. Jay Gupta, Dr. Carol Haft, Dr. Albert Hwa, Dr. Teresa Jones, Dr. Maren Laughlin, Dr. Jean Lawrence, Dr. Yan Li, Dr. Hanyu (Maggie) Liang, Ms. Kate Libit, Dr. Barbara Linder, Dr. Chris Lynch, Mr. Louis Martey, Ms. Mansi Mehta, Mr. Michael Mensah, Mrs. Sarah Neser, Mrs. Heidi Otradovec, Dr. Nishadi Rajapakse, Mr. Daniel Rothwell, Dr. Salvatore Sechi, Dr. Corinne Silva, Dr. Lisa Spain, Dr. Pamela Thornton, Dr. Xujing Wang, Dr. Theresa Woo, Dr. Ashley Xia, Dr. Norann Zaghloul

NIDDK/NIH Staff: Dr. John Connaughton, Mr. Mitch Curling, Dr. Latha Malaiyandi, Dr. Karl Malik, Mr. Paul Myers, Dr. Reaya Reuss, Dr. Griff Rodgers, Mrs. Mary K. Rosenberg, Dr. Elena Sandovich, Dr. Katrina Serrano, Dr. Elain Sierra-Rivera, Ms. Stephanie Thornton, Ms. Erica Thorpe, Ms. Yen Trang, Mr. Phi Truong, Mr. Burnel Wilkins

Council Member Status (Dr. Cefalu)

Dr. Cefalu welcomed DEM's two new council members noting that Ms. Neicey Johnson was recently appointed, and Dr. Carmella Molina-Evans is in the final stages of full approval and was attending this time as an ad- hoc council member. Dr. Cefalu then thanked council member Dr. Philipp Scherer for his service.

Heterogeneity of T2D Working Group of Council: Emerging Recommendations (Dr. Cefalu)

Dr. Cefalu presented an update on the Heterogeneity of T2D Working Group of Council. He noted that the working group has developed an infrastructure with five subgroups, each addressing a specific focus, that have been meeting regularly. Two cross cutting themes, data science and health equity, have also been established, and partnerships and cost-effectiveness are being discussed as future cross-cutting themes.

The working group has over 70 investigators from approximately 13 countries involved, with 20 program staff, five analysts, and three contractors. The expectation is a draft report provided to the Executive Committee in December 2024. Dr. Cefalu then went on to share examples of emerging recommendations, rationale, and opportunities from the five subgroups: Pre-clinical, Clinical, Lifestyle, Engagement, and Innovation.

Two or three preliminary recommendations were highlighted for each subgroup. Dr. Cefalu then went on to state that five to eight recommendations or more are expected from each subgroup, with opportunities of how each recommendation might be addressed for each. In addition to the December draft, he expects that the co-chairs will present the recommendations to the full Council in January 2025. Dr. Cefalu then thanked the Program Directors, co-chairs, and Dr. Scherer for their roles in this endeavor.

Dr. Elizabeth Seaquist mentioned that she is impressed and enthusiastic about the progress of the working group and commended the members. Dr. Scherer added that this has been a very insightful process, and that he is confident that the report will bring all the work of the various working groups together on schedule, and Dr. Cefalu agreed.

Centers for Diabetes Translation Research National Enrichment Activities (Dr. Gorospe)

Dr. Gorospe presented an update on the National Enrichment Program (NEP) conducted by the Centers for Diabetes Translation Research (CDTR), recently funded by an administrative supplement, on behalf of himself and Drs. Thornton and Artis Dickerson. He explained that CDTRs support translational research in diabetes, particularly from bedside to community settings and population studies, using the P30 funding mechanism to support research core resources.

The required components of a CDTR award include an administrative core, at least two translational research cores focused on health disparities or health equity, a pilot and feasibility program for early-stage investigators (ESIs), and an enrichment program for scientific and professional development. The budget is capped at $400K annually, with opportunities for expansion through national and regional resource cores and a national enrichment program.

Currently in its third funding cycle, the program focuses on health equity research and involves numerous partnerships across states. There are seven national or regional cores and 17 local cores, with various cross-center activities. Leadership includes 12 directors, with 50% women and 50% physician-scientists with public health expertise. Two CDTRs follow a multi-PI model.

As preliminary proof-of-concept assessing the structure/content and utility of a National Enrichment Program (NEP), ESI sessions were held during the annual CDTR Directors' meetings of 2020, 2021, and 2022. Feedback from these sessions led to an administrative supplement call in July 2023. The DREAMS-CDTR from California successfully applied and aimed to: (1) create a community of practice for ESIs, (2) organize a national ESI meeting, and (3) disseminate findings. The June 2024 NEP meeting at Stanford University (Redwood City Campus) had over 50 participants, including 35 ESIs and 18 faculty members from 23 institutions, with three from minority-serving institutions. The program included sessions on networking, professional development consultation, and scientific input. A panel discussion with NIDDK Program Officials and ESIs who have recently received NIH awards also took place on the topic: How to Get Your First Major NIH Award.

Dr. Gorospe also provided updates on the community of practice, which now includes 65 ESIs from 30 institutions, and dissemination efforts including a manuscript concept approved for submission to *Diabetes Care* that will detail insights gained from the 2024 NEP meeting. He then presented on the outcomes, lessons learned, and next steps for the CDTR NEP.

Dr. Laughlin then asked how expandable this program is, and if ESIs from many other fields would be able to participate, and Dr. Gorospe said that there are already ESIs from different fields involved. He added that this is not centered solely on CDTR members and that it is open to ESIs from other institutions in different fields. Dr. Cefalu commended the organizers and asked

about the gaps that were discussed. Dr. Gorospe replied that there was not a discussion on a scientific theme, but there was much discussion about health equity. Dr. Molina-Evans asked if there were non-K awardees, or those working on obtaining a K award in the mix, and Dr. Gorospe replied that most attendees were working on submitting a K award soon and did not have one yet. She continued that she noticed that at her own institution that many ESIs were not invited to visit many places and was wondering if there was a possibility of sponsorship so that ESIs might meet other scientists at other institutions. Dr Gorospe replied that that is something that they will consider for the renewal.

DEM Initiative Concept (Dr. Hwa)

Dr. Hwa began his presentation on a new FY26 Initiative, Collaborative Awards to Support Microphysiological System (MPS) Pilot Studies in Type 2 Diabetes Research, a joint effort developed with Dr. Haft. He gave a quick overview of MPSs which are *in vitro* systems that re-capitulate higher orders of cell/tissue organization, emulate human physiology, and allow disease modeling and drug discovery studies. There can be membrane configurations for layered tissue organization, and allow for more physiological, 3D organization that contain more than 2 cell types. They may also include other features, such as mechanical force control and fluid flow connecting multi-tissue compartments that allow for the study of diabetes as a multi-organ disease and can be used in conjunction with animal models.

He highlighted that the proof of concept for MPS has been successfully demonstrated, and a workshop on MPS in type 2 diabetes research was held last September which discussed this. Over the past five years, the NIDDK has supported a consortium dedicated to modeling type 2 diabetes using MPS. Key achievements include deriving metabolic tissues from stem cells and establishing them in MPS devices. These studies have shown baseline tissue-specific physiology, simulated metabolic dysfunctions, and molecular transport between tissues. MPS exhibit high potential for studying human type 2 diabetes, including aspects such as sexual dimorphism, heterogeneity in clinical responses, and known endocrine communication mechanisms. Dr. Hwa also discussed several challenges encountered in the development and use of multi-cell type and multi-tissue systems, such as the lack of universal multi-organ culture media and the high cost and complexity of MPS technologies. To overcome these hurdles and make MPS more accessible, collaboration between biology and engineering labs is essential. The ultimate goal is to establish comprehensive MPS that cover all aspects of type 2 diabetes development, prevention, and treatment. Achieving this ambitious goal will require large teams, substantial funding, and extended development timelines.

To facilitate the adoption of MPS by diabetes researchers and to build a runway for future R01s, staff propose creating small pilot research awards to support lab partnerships in applying existing MPS to critical research questions, conducting feasibility studies, and generating preliminary data. Two receipt dates will be available, allowing researchers to revise and resubmit proposals if not funded in the first round. A focused review panel convened by NIDDK will evaluate applications, ensuring balanced assessments by both biology and engineering experts. Additionally, there are plans to update small business grant language to encourage the use of commercialized MPS prototypes through SBIR and STTR grant mechanisms.

Dr. Hwa outlined several potential research topics, including complementing existing animal and human models to demonstrate the relevance of human T2D physiology, validating aspects of type 2 diabetes pathophysiology, and demonstrating system durability and compatibility to allow the confirmation of tissue crosstalk communicators.

Dr Hwa then opened the floor for questions and comments. Dr. Scherer highlighted the limitations of individual systems but noted the unique opportunity to study inter-organ crosstalk extensively. Dr. Cefalu and Dr. Scherer agreed that this could be useful to mention in the recommendations of Heterogeneity of Diabetes pre-clinical working group. Dr. Haft mentioned that there was a discission at the workshop on the potential of using human induced pluripotent stem cells (iPSCs) to compare different individuals' tissues, which could be resource-intensive but valuable. Dr. Scherer touched on the historical progression of MPS technology and its potential to understand genetic diversity in diabetes responses. Dr. Cefalu reiterated that this could be included in the first recommendation of the preclinical subgroup. Dr. Molina-Evans emphasized the importance of standardizing assessments within any consortium formed through these awards to ensure consistent and reliable results. Dr. Hwa mentioned that the second recommendation of the preclinical subgroup also mentioned the importance of metabolic assay standardization. Dr. Haft mentioned that it is very difficult to get standardized measures, but it is a very good goal. Dr. Spain mentioned that she and Dr. Hwa wrote a paper in Nature Reviews Bioengineering that encourages NIH grant applications on collaborative science.

DEM-Sponsored Workshops and Activities of Interest (Dr. Cefalu)

Dr. Cefalu introduced and presented on future workshops for DEM. He then congratulated Dr. Burch on the success of the Application of Digital Health Technology to the Management of Type 2 Diabetes workshop. Dr. Haft noted that the 2024 Annual Mid-Atlantic Diabetes and Obesity Research Symposium is a result of the ongoing collaboration between NIDDK intramural investigators and extramural colleagues.

- The Application of Digital Health Technology to the Management of Type 2 Diabetes
  - September 5-6, 2024
  - Hybrid: Building 31, NIH Campus, Bethesda, MD/Virtual
- NIDDK Centers for Diabetes Translation Research Directors' & Network Annual Meeting
  - September 17-18, 2024
  - Two Rockledge Center, 6701 Rockledge Drive, Bethesda Maryland
- 2024 Annual Mid-Atlantic Diabetes and Obesity Research Symposium
  - September 27, 2024
  - Hybrid: Natcher Auditorium, NIH Campus, Bethesda, MD/Virtual
- Implementation Science and Health Equity: An NIDDK Workshop
  - October 10-11, 2024
  - Hybrid: Natcher Auditorium, NIH Campus, Bethesda, MD/Virtual
- Artificial Intelligence in Precision Medicine of Diabetes and Other Chronic Diseases
  - October 30-31, 2024
  - Hybrid: Neuroscience Center, 6001 Executive Blvd, Bethesda MD/Virtual
- Diabetes Mellitus Interagency Coordinating Committee Meeting on Research Supported

- by the Special Statutory Funding Program for Type 1 Diabetes Research
    - November 12, 2024
    - Natcher Auditorium, NIH Campus, Bethesda, MD
- A 10-Year Anniversary Symposium Organized by The Human Islet Research Network: Changing the Course in Type 1 Diabetes
    - January 13-14, 2025
    - Natcher Auditorium, NIH Campus, Bethesda, MD

Concluding Remarks (Dr. Cefalu)

Dr. Cefalu thanked the Sub-committee members and DEM staff for their presentations and comments. He noted that DEM looks forward to providing details at a future meeting on the progress made on the programs discussed today. Dr. Cefalu noted that new ideas and suggestions are always welcome.