

221st NIDDK Advisory Council Meeting
Division of Diabetes and Endocrinology and Metabolic Diseases (DDEMD)
Sub-committee Meeting – Open Session
January 25, 2023

Attendees

DDEMD Sub-committee Members: Dr. David D’Alessio, Dr. Debra Haire-Joshu, Ms. Davida Kruger, Dr. Philipp Scherer, Dr. Elizabeth Seaquist, Dr. Michael Snyder

DDEMD Staff Members: Dr. Kristin Abraham, Dr. Beena Akolkar, Dr. Guillermo Arreaza-Rubin, Dr. Shavon Artis Dickerson, Dr. Raj Basu, Dr. Miranda Broadney, Dr. Henry Burch, Dr. Art Castle, Dr. William Cefalu, Dr. Maureen Monaghan Center, Dr. Brad Cooke, Dr. Thomas Eggerman, Dr. Rafael Gorospe, Mr. Neal Green, Dr. Carol Haft, Dr. Albert Hwa, Dr. Teresa Jones, Dr. Maren Laughlin, Dr. Jean Lawrence, Dr. Ellen Leschek, Dr. Yan Li, Dr. Barbara Linder, Dr. Karl Malik, Dr. Saul Malozowski, Mr. Louis Martey, Ms. Mansi Mehta, Mr. Michael Mensah, Mrs. Heidi Otradovec, Dr. Salvatore Sechi, Dr. Corinne Silva, Dr. Lisa Spain, Dr. Pamela Thornton, Dr. Xujing Wang, Dr. Theresa Woo, Dr. Ashley Xia, Dr. Norann Zaghoul

NIDDK/NIH Staff: Mr. Terry Barnes, Dr. Najma Begum, Dr. John Connaughton, Dr. Ann Jerkins, Dr. Karl Malik, Mr. David Robinson, Dr. Paul Rushing, Dr. Elena Sandovich, Dr. Thomas Tatham, Ms. Yen Trang

Welcome and Approval of September 2022 Sub-committee Minutes (Dr. Cefalu)

Dr. Cefalu welcomed everyone to the DEM Sub-committee Open Session meeting and provided an overview of the agenda. Minutes were moved for approval and approved by committee members. He then introduced and welcomed two new DEM program directors, Dr. Raj Basu, and Dr. Rafael Gorospe, as well as acknowledged Dr. Michael Snyder for his council service extension.

Heterogeneity of T2D Working Group of Council (Dr. Zaghoul)

Dr. Cefalu introduced Dr. Zaghoul who presented on the Heterogeneity of T2D and the role of a soon to be formed Working Group of Council (WGoC). She provided a general overview of the working group and how their work will align with NIDDK’s strategic plan’s goal of understanding disease heterogeneity. She then provided an overview of several recent approaches being used to assess T2D heterogeneity including “hard clustering”/distinct subgroups, molecular profiling of T2D clusters/ IMI RHAPSODY study, using genetics toward classification of T2D, “Palette Model” of T2D/spectrum of disease, and “soft clustering”/overlapping subgroups in IMI-DIRECT study. Dr. Zaghoul then led the group in a discussion on what the initial priorities should be for NIDDK’s T2D heterogeneity efforts, what role the WGoC could play in informing NIDDK efforts for reclassifying diabetes, and what areas of expertise are not well-represented in current heterogeneity efforts and should be incorporated into WGoC.

Dr. Snyder noted that inexpensive digital readouts are important, and their utility should be considered by the working group. Dr. Snyder also added that longitudinal data should be gathered in the study of T2D heterogeneity including early-stage prediabetes. Dr. Seaquist echoed and emphasized that a good understanding of pathophysiology should be a focus. She

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also noted that an individual with expertise in environmental exposure would be advantageous to include in discussions. Dr. Scherer agreed with the comments stated by other council members and added that a limited number of subtypes/biomarkers should be identified as a goal for this working group. Dr. Haire-Joshu emphasized that she appreciates this effort and is eager to see what the research yields. Dr. Seaquist added that this is a good opportunity to utilize health system data to get information about all the people with T2D to follow prospectively moving forward. Dr. Haire-Joshu further added that having additional expertise around social determinants and equity are key, as well as gaining input from community members. Dr. D'Alessio stated that too many clusters may be a detriment to this research effort and should be identified prior to the start to maintain an effective study. Dr. Cefalu stated that the formation and charge to new WGoC will begin soon keeping in mind the points raised by council members; feedback/updates will then be provided at future council meetings.

Diabetes Centers Research Centers (Dr. Silva)

Dr. Cefalu introduced Dr. Silva who presented on the Diabetes Research Centers (DRCs). She provided a general overview of the DRCs and reviewed the DRCs' history, mission, structure, the NIDDK/DEM centers program budget, the DRCs currently funded, plus challenges, strategy, and plans for the program in 2025 and beyond.

Dr. Scherer asked how NIDDK views the interplay between all the various NIDDK Center programs; what can be done to enhance the synergy between programs at institutions. Dr. Silva responded by saying an evaluation was conducted back in 2010 that yielded a report that supported the need for increased collaboration and synergy scientifically among the DRCs. NIDDK agrees about the need for synergy and collaboration among DRC institutions and is open to feedback on how to improve this relationship. Dr. Cefalu echoed DK's desire to improve these relationships with the DRCs. Dr. Seaquist emphasized the need for adaptation as the centers have changed significantly over the years, especially considering the pandemic. Ms. Kruger raised the point of focusing on bringing on the next generation to work side by side with and prepare for succession of the existing DRC network. Dr. Silva stated that NIDDK is interested and willing to address this issue. Dr. Cefalu echoed NIDDK sentiments and acknowledged that DK has an obligation to train the next generation. Dr. Scherer noted that DRCs robust and effective funding/spending/success has aided in its longevity over the years. Dr. Snyder agreed with Dr. Scherer's comments. Dr. Haire-Joshu commented on the theme of synergy as being a good concept/goal to pursue and suggested taking different approaches, structurally and transitionally, to achieve the synergy goal.

Type 1 Diabetes TrialNet (Dr. Spain)

Dr. Cefalu introduced Dr. Spain who presented on the T1D TrialNet. She provided a general overview of the program and reviewed the goals, framework for progression of T1D, TrialNet organization, TrialNet studies and trials, teplizumab treatment of those at high risk, key mechanistic questions, TrialNet pipeline, expert panels, and questions for TrialNets's future. Dr.

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Spain also discussed questions related to TrialNet's future including what the impact of Teplizumab's approval on TrialNet participation will be, how future trials will be designed and on the availability of agents to test. Discussion was held on how communication about TrialNet's results and research opportunities could be enhanced, optimizing opportunities for collaboration for T1D prevention, and whether TrialNet's organization/structure is sufficient to achieve its goals for the future.

Dr. Cefalu highlighted the success of the program but made note of the challenges to address ahead. Dr. Snyder asked a question about research related to CAR-T therapy for rheumatoid arthritis and its potential application to TrialNet studies. Dr. Spain responded that this is an exciting emerging field of research that is not in the program at this time but could be considered as the research progresses. Ms. Kruger commented that in her clinic, she would appreciate more guidance to help endocrinology clinics use of teplizumab now that it is approved. Dr. Spain noted that TrialNet investigators may produce a paper to help illuminate the TrialNet role and experience with teplizumab. Dr. Cefalu asked Ms. Kruger about her clinical practice and participation in TrialNet trials and Ms. Kruger explained that they have not significantly participated in the TrialNet program, however moving forward she would like to do more. Dr. D'Alessio commented on the impact of TrialNet's longitudinal pathology of disease data which has been a backbone of the trials and wanted to know if the program could expand on this breadth of knowledge. Dr. Spain responded by saying there is a lot to learn about T1D risk factors related to environment and genetics as it pertains to TrialNet populations, and that TrialNet has collaborative opportunities for investigators.

Review of Council Feedback on the Presentation: The Application of Digital Health Technology to the Management of Type 2 Diabetes (Dr. Burch)

Dr. Cefalu introduced Dr. Burch who provided a summary of Council member feedback to the presentation at October 2022 Council of the topic: Digital Health Technology for the Treatment of Type 2 Diabetes and reviewed the needs, goals, tools, and barriers to helping to managing T2D with digital health technology, as well as, topics related to stakeholder engagement, the digital divide, research methodology, interoperability, implementation, intervention targets and outcomes, industry partnerships, funding mechanisms, and next steps.

Dr. Burch had organized Council member commentary from October Council into specific comments grouped broadly into 9 categories ranging from stakeholder engagement to the digital divide and partnerships with industry. The review was appreciated by council members, who voiced the following final comments.

Dr. Snyder is supportive of this effort and noted that the health data for T2D management is inexpensive to collect and only added that it would be nice to have the data collected earlier in prediabetes. Dr. Haire-Joshu is also supportive of this effort and emphasized stakeholder engagement and implementation efforts as major focus areas moving forward. Dr. D'Alessio took the issue up with his medical director who noted that there is not enough connection/integration between wearable data and EHR systems. Dr. Seaquist supported AI

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involvement in this effort and suggested that shared decision making, and patient preference should be included in the AI model to ensure appropriate care for the patient. Dr. Snyder suggested that industry should be invited to the next workshop and Dr. Burch responded that there are plans for industry involvement moving forward.

DEM Training and Career Development Update (Dr. Castle)

Dr. Cefalu introduced Dr. Castle who presented on the DEM Training and Career Development Update. He provided a general overview of the DEM Training and Career Development and reviewed the training timeline, training program concerns, research workforce/future needs, fewer post docs and other unfilled positions, recruitment and retention of post docs efforts and supporting the careers of emerging investigators.

Dr. Scherer noted that the post doc crisis at his institution is starting to improve as industry begins to grow saturated. Dr. Scherer asked why fewer applications have gotten funded recently and Dr. Castle responded by saying stipend increases and child support affects the number of slots available for applications. He added that more funding would be needed to fund more post docs. Dr. Snyder commented that he would like to see more publicity/outreach/marketing with the post doc awards and wanted to know if NIDDK has been more negatively affected by the post doc crisis relative to the rest of the community. Dr. Castle responded by saying the division has been more adversely affected but cannot say that NIDDK has been more negatively affected than any other ICs and noted that K99 applications have improved to some degree over the years in comparison. Dr. Spain supported Dr. Castle's comments related to the K applications and noted that it is exciting to see the program's progress. Dr. Haft noted that KUH is currently piloting the use of a F99/K00 training grant mechanism to bring new people into KUH research areas. Dr. D'Alessio acknowledged the post doc crisis internationally and noted the general struggle of institution's efforts to acquire post docs. Dr. Seaquist added that her division is also having trouble filling slots as well and has found it particularly difficult to find MDs who are interested in doing research. She noted that this is related to international graduate ineligibility and lack of loan repayment awareness benefits among potential candidates. Dr. Haire-Joshu echoed the sentiments of other members related to recruitment. Dr. Castle received all feedback given during the presentation by council members and reiterated that changes will need to be made to remain competitive in this research space amongst outside sources. Dr. Spain advertised the K12 5-year program which was rolled out this past fall and is now a National K12 program. She encouraged advertisement and recruitment of any potential candidates.

DEM Workshops (Dr. Cefalu)

Dr. Cefalu introduced and presented on future workshops for DEM:

- Neural Plasticity in Energy Homeostasis and Obesity
 - April 13-14, 2023
 - Virtual
- NIDDK K Awardees' Workshop

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- April 20-21, 2023
- Lister Hill Center Auditorium (Building 38A)
- Bethesda, MD
- Fifth Artificial Pancreas Workshop
 - May 1-2, 2023
 - Bethesda, MD
- Microphysiological Systems (MPS) for Studying T2D, Obesity, and Their Complications
 - Fall, 2023
 - 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.